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THE AMERICAN
JOURNAL OF PHARMACY

MARCH, 1919

EDITORIAL.

THE POSITION OF THE COMMITTEE ON EDUCATION AND SPECIAL TRAINING IN REGARD TO S. A. T. C. UNITS IN SCHOOLS OF PHARMACY.

Under the above title there is printed in the "Correspondence" in the February number of the *Journal of the American Pharmaceutical Association* the following letter.

WAR DEPARTMENT.

Committee on Education and Special Training, Section of Training and Instruction Branch War Plans Division, General Staff.

January 18, 1919.

CHARLES H. LAWALL, *President,*
American Pharmaceutical Association,
39 South 10th Street, Philadelphia, Pa.

Dear Sir: You have requested, as President of the American Pharmaceutical Association, a statement of the position of the Committee on Education and Special Training in regard to S. A. T. C. units in schools of pharmacy. The basis of this request is that the subject has been under discussion by many who are interested in education in pharmacy and in the pharmaceutical journals, and that it is not clear that the position taken by the War Department has been fully understood. With the permission of the Chairman of the Committee on Education and Special Training the following statement is made:

The object of the Students' Army Training Corps was to furnish a supply of educated men from whom officers for the new army could be chosen, and to direct their training while in educational

institutions so that those selected for commissions would more quickly be prepared to assume their duties as officers. It was strictly a war measure, and not an attempt by the government to standardize education. Any effect this plan may have had on the problems of education in any line in peace times is entirely incidental, and this matter received consideration only to the extent that it was the aim of the committee to disturb existing methods of education as little as was consistent with the attainment of its aims.

In the case of pharmacy the fundamental consideration was that the needs of the Army for pharmacists would be satisfactorily met through the draft. Although there was no real necessity for the inclusion of pharmacy students in S. A. T. C. for the purpose of supplying pharmacists for the Army, the Committee, nevertheless, decided that a limited number might wisely be accepted on the basis that this training would also prepare them for service as chemists and in other useful capacities. The plan finally evolved was to recognize those pharmacy schools in institutions which already had S. A. T. C. units, and to limit the admission to those students in these schools who were eligible for the collegiate section. This required graduation from an approved four-year high school, or an equivalent education.

A committee of representative educators in pharmacy, chiefly from the schools which would be eligible under this plan, was consulted September 29, 1918. This committee was requested to draw up a sample course in pharmacy. As in the case of all programs for courses adopted by the committee, this program in pharmacy was not prescribed but was issued as an example of what would be acceptable.

Yours very truly,

Committee on Education and Special Training,

(Signed) By H. D. ARNOLD,

Lieut.-Colonel, Medical Corps, U. S. A.

HDA/MNN

The appearance of this *official* statement of the position of the War Department concerning the Students' Army Training Corps units in pharmacy schools and the purpose that actuated the Department in the establishment of these, is welcomed as a conclusive justification of the editorial "A Quasi Recognition of Pharmacy."

published in the November, 1918, issue of the AMERICAN JOURNAL of PHARMACY.

The previously announced position of the then Surgeon-General Gorgas "that the needs of the Army for pharmacists would be satisfactorily met through the draft," is repeated in this official statement and was reflected in the actions of the Committee on Education and Special Training. The decision of the committee to include in the S. A. T. C. the "limited number of students in those pharmacy schools in institutions which already had S. A. T. C. units" and "on the basis that this training would also prepare them for service as chemists and in other useful capacities," indicates that the acceptance of such pharmacy students was incidental and that the real object was "service as chemists and in other useful capacities." In no way can this be construed as a direct and distinct recognition of pharmacy and the language of this offical statement bears out fully our characterization of "quasi."

The statements made in certain articles that have appeared in the pharmaceutical journals such as these: "pharmacy had thus been recognized by the government as a profession," "this is a very satisfactory recognition of professional pharmacy," "here, at least, pharmacy came into its own and received the same recognition as was accorded to the other professions," and "the War Department recognized the need of establishing a pharmacy unit in the S. A. T. C. in order to train men for army and civil life," are unfortunately for pharmacy not verified by the facts. The statement made in person to the writer by an official in the Department was that if pharmacists were, really, the need the first consideration would have been given to schools that were not included in the S. A. T. C.

Furthermore, this *official* statement refutes the claim that "the federal government has set a standard for pharmacy." In dulcet tones this theme has been harped upon and spread widecast by those whose desires it would appear had obtunded alike their view of the true situation and their sense of propriety. The object of the S. A. T. C. was to furnish the many thousands of officers that would be needed for the army contemplated, and this should have been well known to all. The body blow to these sentimental strains is now administered by the positive assertion in this letter that: "It was strictly a war measure, and not an attempt by the government to standardize education. Any effect this plan may have had on the

problems of education in any line in peace times is entirely incidental, and this matter received consideration only to the extent that it was the aim of the committee to disturb existing methods of education as little as was consistent with the attianment of its aims."

It is not the intention to continue the polemics displayed in the editorial correspondence in the January issue of the JOURNAL, but this letter of the War Department substantiates our editorial contention so well that its publication was deemed necessary along with a minimum of comment which could also have been greatly amplified. Doubtless the readers who are interested in this question will appreciate the quod erat demonstrandum.

G. M. B.

PHARMACOPŒIAL REVISION.

The attention of the readers of the AMERICAN JOURNAL OF PHARMACY is directed to a circular letter issued by the Chairman of the Committee of Revision of the Pharmacopœia of the United States published on page 185, requesting that suggestions for corrections, improvements, additions, etc., should be sent to him. The intent is to compile all of these recommendations for presentation to the convention to be called for the Tenth Decennial Revision for the benefit and use of the committee to be then selected for that revision of our national authority for standards.

This is a very timely communication and this appeal for coöperation should be very generally responded to. It is very creditable to the efforts and a testimony to the effectiveness of the service rendered by the Committee of Revision that prepared the Ninth Revision, that so few errors in the text have been found and so few of the standards have been seriously criticized. It has likewise withstood the test of the unusual conditions prevailing throughout the last four years and the period of the world war. Very few indeed have been the changes or corrections required to be made, and it has not been necessary for the committee to issue the Supplement that they were given authority to publish. However, all works of human hands and the minds of men are more or less imperfect and the new knowledge and the new medicines coming into use and others becoming obsolete from disuse are ample reasons that have justified the wisdom of the American method for a decennial revision of our pharmacopœia.

The AMERICAN JOURNAL OF PHARMACY has always been a prime mover in aiding in the various revisions of the U. S. P. and its pages have contained many papers that have been of very material assistance to the committees that have been charged with the responsibility of preparing the various revisions. No better medium for the presentation of subjects for pharmacopœial consideration is offered and its columns continue to be open for such matters and especially welcome are papers containing recommendations for amendment or improvement in the official formulas or standards.

It is opportune to call attention at this time to the fact that the next United States Pharmacopœial Convention is scheduled to meet in the city of Washington in May, 1920. As many of the medical, pharmaceutical and chemical organizations, who are properly represented in this convention, will hold their meetings for 1920 after the date named, these organizations should not fail to select their accredited delegates at their various meetings held during the present year. The importance of membership and representation in this convention should not be overlooked.

G. M. B.

THE STUDY OF DRUGS.

BY DR. FRED. B. KILMER.

The advice of the most successful men in our calling is to "stick to drugs." Keep drugs and medicinal appliances to the forefront. Let your customers know that you keep a drug store. Put in side lines when you find that they will pay, but use them to increase your regular trade.

The people of the United States, in congress assembled, have defined the word "drugs" to mean all medicines and preparations recognized by the United States Pharmacopœia, or the National Formulary, for internal or external use, and all substances or mixture of substances intended to be used for the cure, mitigation or prevention of disease, either of man or animal.

This literally means that every substance that can in any way whatever be used in medicine or in surgery, belongs to the drug store. The range is large enough to tax the capacity of the ordinary pharmacy. It is for the drug trade to get, and to hold fast to, that which belongs to it.

To the man who bewails that there is no future in pharmacy, to the young man looking for an opening, I commend a study of the foregoing definition of drugs, as a possible chance to secure a foothold for himself and to "cash in" on his diploma. In other words, I commend to him a study of drugs.

Materia medica and therapeutics today present a broader and a wider field than ever before in their history. Drugs need more than ever the careful study of the trained mind of the pharmacist. Pharmacy is not the selling of cigars, soda water, confectionery, stationery and knick-knacks, although it is true that these may by force, form a part of the modern stock, and must be dealt in to keep the business going. Pharmacy is not the simple selling of drugs, or handling them over the counter in prepared packages. Real pharmacy is the integral part of the great science of medicine and surgery, and has to do with all the allied applications of the healing art. Yea, it even extends out to, and has to do with, hygiene, and the wonderful coming forme of preventive medicine.

The pharmacist should know, from its beginning, every substance in any way connected with the application of these sciences. He should know them from a to z, in their every aspect. How else can he be a pharmacist, or become a master of his calling?

He should know drugs, and all there is to be known about them. Ordinarily the pharmacist learns, either in his apprenticeship or the college, the names of the most commonly used drugs, and the preparations made therefrom. Perhaps he memorizes the doses of potent drugs. The rest of his knowledge is gained from the label, or a quick reference to the Dispensatory, or to the manufacturer's catalogue.

Few pharmacists, especially the younger men, have a thorough knowledge of even a quarter of a hundred drugs. How many can speak, upon their own authority, as to the pharmacology and the therapy of any appreciable percentage of the drugs which they handle every day?

Here then is an opening in pharmacy—the study of drugs. That the pharmacist should know the pharmacology of drugs, will probably not be questioned. But the objection may be made that emphasis laid upon the therapeutic action of drugs by the pharmacist has a tendency to counter prescribing. The reverse is probably true. Counter prescribing is now most largely carried on empirically, by

men who have only a superficial knowledge of drugs, and with whom it is often a matter of chance and extensive guessing.

The pharmacist who has a real knowledge of pharmacology, and the therapeutic action of drugs, would probably be the last to prescribe. To know even the physical characteristics of a drug, its active principles, its constitutional formula, its dose, without knowing its uses, its functions, its effects upon the system in health and in disease, is like knowing the names of the organs of the body without knowing their functions.

Who shall know drugs except the pharmacist? The physician's knowledge of materia medica in a large number of instances is not profound. During his college course, at the present day, he can give materia medica and therapeutics but scant attention. The limited hospital pharmacopœia and the manufacturer's literature often make up his library. He has no time or opportunity to really study drugs.

A knowledge of drugs would enable the pharmacist to extend the physician's materia medica, to assist him in choosing the right form, to realize his intentions, and it might help him to overcome the medical man's habit of office dispensing of a limited number of drugs. Even a conversational knowledge, covering the range of conventional and recognized drugs, would help to fill the physician's prescription with really useful preparations.

A knowledge of drugs makes a pharmacist a pharmacist, places him in his right position—a master of his profession—a position that the medical profession and the public are bound to recognize, and from which he cannot be dislodged.

Here is a list of drugs, the most of them in quite common use: aconitum, aloes, ammoniacum, arnica, belladonna, cannabis, indica, capsicum, cascara, cinchona, conium, digitalis, ergota, gelsemium, hydrastis, hyoscyamus, ipecacuanha, jalapa, krameria, lobelia, nux vomica, opium, podophyllum, rheum, senega, serpentaria, stramonium, sumbul, valeriana, yerba santa.

Let us ask ourselves a few questions about them. It will be especially good practice for the student.

Without consulting a text-book, could you describe their characteristics as to appearance, taste and odor?

If they were laid out on a table, unlabeled, could you recognize and name them?

What are their chief therapeutic properties?

These are simple, almost foolish questions. Any junior in college ought to be able to answer them. Young men "cram" up on these very drugs in order to pass the board of pharmacy.

Now, let us see all that we know, all that everybody else knows, and maybe we will come to the conclusion that there is much yet to be found out about these everyday drugs; that there is in many of these commonplace substances opportunity for long and earnest study, opportunity for the pharmacist to make a name for himself, to do a great work for the science of pharmacy and medicine, and bestow untold benefits upon his fellow-man.

Let us take up one or two of them in alphabetical order:

Aconite.—The books say it contains the powerful principle, aconitine. Its chief characteristic properties are defined as "anodyne, diaphoretic, sedative; a powerful sensory nerve stimulant." Page after page in the books tells of its origin, history, structure, chemical composition, pharmacology, physiological action, uses, doses, etc. Knowledge beginning in the far distant past, accumulated, recorded and handed down to us. Incidentally, we find there are a number, but not quite "57," varieties of aconite and while the books don't say which is which, the species know as aconitum napellus is official, and for the most part the value of the other sorts is not recorded. Possibly some of the other kinds are "just as good," maybe they are better—who knows.

A test laid down for the so-called powerful principle is to take a piece of aconite root, chew a bit of it, and there results a peculiar tingling or numbing, quite appreciable on the tongue and roof of the mouth.

Aconite grows in the temperate zones of the northern hemisphere, including the United States. (It is cultivated in gardens.)

Find the growing plant and chew a piece of the fresh root. You will notice first a sweet taste, and the odor of radish. Upon chewing for a time, aided by the action of saliva, the tingling and numbness appears. On drying the root, the odor, color and taste change.

The so-called active principle is evidently not in evidence in the growing plant. Question: Is this powerful principle developed in drying the plant? If so, would the method of handling and drying influence the character and the amount?

The pharmacopœia, and other books, set forth certain preparations of aconite, and tell us how to prepare them. Powders, pills, tinctures, fluid extracts, solid extracts, liniments, etc.

Which of these preparations most truly represent the anodyne, diaphoretic and sedative properties of the drug?

Experience has shown that some of them are unreliable, in that they are highly active under some conditions, as under other conditions, some of them are practically inert. Which of these preparations would you advise a physican to choose as best exhibiting any one of the three characteristic properties? Which is the best for anodyne effects? Which for diaphoretic effects? Which for sedative effects? Which of these preparations represent the whole drug? Which will give the results the prescriber seeks for?

Let us pass on to *aloes,* a drug known and used in medicine centuries before the Christian era. The books teem with words about it. We learn that solidified juices of the leaves of various aloe are the sources of the several varieties of aloes. We read that its most potent principle is a rather variable substance called "aloin." That from aloes the chemists have separated a number of remarkable substances—resinous, crystalline, amorphous, extractive and the like.

The characteristic actions of aloes, we learn, are defined as "cathartic, hepatic, stimulant." That in small doses it acts as a stomachic, in large portions as an emmenagogue.

How much do we, as pharmacists, know of the difference in action between the several varieties of aloes? What have we determined as to whether the crude methods by which the juice is gathered and prepared, have any influence upon its action? Which of our preparations best exhibits the action of aloes as a cathartic or hepatic stimulant? Which preparation is best when a stomachic is desired? Which when an emmenagogue is wanted? Which preparation represents aloes in all its phases? Do our preparations take into account the aloin or the many resinous and crystalline derivatives found in aloes?

Now let us consider *belladonna.* This is one of the most ancient drugs known to medicine. Thousands upon thousands of pages, and hundreds of volumes, have been written about it. All through the ages belladonna has grown more prominent, and stands today as one of the most useful drugs in materia medica. Any graduate in pharmacy could write a thesis on belladonna, and would possibly claim (at least at graduation) that he "knows all about it."

What do we know? What does anybody know? What is the sum of our knowledge of belladonna?

The things which a pharmacist ought to know about belladonna are delineated in the Pharmacopœia and the Dispensatories, and I advise every young pharmacist to read carefully what these have to say about belladonna. The history of the drug is a most interesting study from every point of view. It would take too long to attempt to describe here the chemical, pharmaceutical and physiological properties of this drug. It has a stated action. It is an anodyne, anti-spasmodic, stimulant, anti-sudorific and mydriatic. It has effects, peculiarly its own, on the nervous system, the respiratory system, the glandular system and the secretive system, and this action exists when taken internally, as a drug, or applied as a plaster.

As pharmacists we are most interested in its active principle What is the active principle of belladonna? The usual answer is "atropine." Is this the correct answer? Investigation has shown that atropine does not exist in cultivated belladonna, nor indeed in belladonna when carefully handled and dried. Atropine is a product, or a derivative, produced during the manipulation of the drug. In assaying belladonna in the laboratory atropine is produced during the process, and is taken as the standard for estimating the alkaloidal value of the drug. Here is a table showing the various constituents which have been found in belladonna by various observers.

Constituents of Belladonna.—Atropine, hyosyamine, belladonnine, atropamine, apoatropine, starch, malic acid, chrysatropic acid, lexatropic acid, succinic acid, prendatorine, phyteumscolla, atrosine, chlorophyl, potassium salts, magnesium salts, calcium salts, sodium salts, ammonium salts, acetic acid, gums, resins, mucilage, asparagin, albumin, etc. This is quite an array. Certainly there is something present in belladonna besides atropine.

There are four or five alkaloidal bodies associated or combined with numerous other constituents, all of which in some measure make up the physiological and therapeutic action of belladonna. It may be stated with confidence that neither a solution of atropine, nor the salts of atropine, seem to possess the full qualities of the extract of belladonna. "Admixtures of extractives with the alkaloid cannot fully replace natural belladonna extractives that are of the same alkaloidal proportions."

Prof. Lloyd has stated: "In my opinion the term 'derivative' will apply better to belladonna ultimates than constituents." All

alkaloidal bodies, possibly, are only derivatives, and atropine is only an artificial derivative which, by common consent, is used as a measure of the drug.

Many problems surrounding belladonna await investigation by the pharmacist. Do the tincture, solid extract, ointment and the like, represent belladonna in its entirety, or are they only solutions of atropine, or some of the other derivatives? Is alcohol the best solvent for the actual constituents of belladonna? If so, what strength alcohol is likely to give the more eligible preparation in every respect—physiological, therapeutic and pharmaceutical? There is much to be learned before we can say that we have reached the top in respect to our galenical preparation of belladonna.

We are now cultivating belladonna in relatively large quantities in this country (possibly 500 acres in 1918), and in this cultivation we have learned something. We can increase the size of the leaf and the root. We can in a measure control and increase the amount of the so-called active principle. We have found that different results follow the handling of the plant from the seedlings to the mature and ripened plant. There is a difference in the physical appearance, size, taste and odor of the plant itself when we vary the mode of collecting and curing. Cured at one stage of growth, when the crop matured, cured at another stage, or gathered at another stage of growth, and allowed to sweat and become subject to enzymic action, gives an entirely different product from that obtained from other modes. Just how important these different methods of preparation may be, or what method is best has not yet been fully determined.

We seem to see that the alcoholic extract of the green leaf is quite different physically from that prepared from the root.

The problems connected with the cultivation of belladonna have been at times baffling. It was not an easy task to acclimatize belladonna from the moist cool climate of Europe, to the dry, hot atmosphere which abounds in our land. It was difficult to inure it to our soil, but we have succeeded in producing thrifty plants with an increased yield of alkaloid principles. American grown belladonna, in most respects, is far superior to the wild product from its native soil. Now comes the task of the study of the pharmacological properties of American grown belladonna.

There is not time to go through the list of drugs given in our schedule; each of these presents a theme for study and research.

Some of them have, since the beginning of the war, been among the list of scarce drugs, and we have been sorely tried with supplies of doubtful origin and usefulness. At times we have been compelled to look for substitutes. We may with profit ask—Which of our preparations best exhibit the physiological and therapeutic properties of the drug? If a drug has more than one action, what preparation represents these separate actions? In making a pharmaceutical preparation of these drugs do we take into account all of the constituents of the drug?

The solvent now most commonly used for vegetable drugs is alcohol. Alcohol is becoming a very expensive solvent and difficult to procure. It may be that there is a better solvent for many drugs. Workers have become convinced that a substance other than alcohol should be found for use as a solvent for many vegetable principles. Possibly we are following precedence rather than actual knowledge in the percentage of alcohol which we use for the extraction of drugs. Here are a few of the problems which will occur to every worker in drugs: Alcohol of 95 per cent. is a solvent for a certain range of constituents. Alcohol 50 per cent. strength gives us an entirely different range of substances. Which percentage is best adapted to each?

If we moisten a pound of the drug with our menstruum, and pack in a tall, narrow percolator and proceed to percolate in the conventional manner, by pouring on the drug a pint of alcohol, we will see that when it proceeds through the drug it becomes loaded with extractive, and its solvent power changes. Its solvent power at the last inch is quite different from its solvent power at the first inch. The second pint of menstruum will be brought in contact with the drug and constituents left behind, or perhaps only partly carried over with the first pint which passed through. With every step every new addition of menstruum, and every new percolate you will have a different action. When we have finally reached the point where we can say we have extracted all of the principles, we find that the menstruum will still dissolve something.

If we take our percolate from the drug made, say with 80 per cent. alcohol, and put the liquid in an evaporating dish and set the dish over a flame and evaporate the menstruum, the result will be a sticky mass which we call the solid extract. This, we say, represents the drug. Now, if instead of evaporating the liquid over the fire we pour it into thin films and allow warm air to drive off

the menstruum, we will again have produced a solid mass which it will be found presents quite a different appearance from the other extraction. In short in subjecting the vegetable drug extractive to prolonged heat we change its character—we cook it, and the delicate vegetable principles all become changed during the process of evaporation and concentration. Lloyd says that in these drugs the so-called alkaloids are in a colloidal form. Undoubtedly prolonged heating will produce a change in vegetable colloids, but as related to medicinal substances no one has fully investigated these changes.

To the younger men of the profession, let me suggest, there is much yet to be developed in the chemistry and the pharmacy of our best known drugs. Let us be pharmacists and devote our most earnest attention to the study of drugs.

BALLOTA HIRSUTA, A RECENT ADULTERANT FOR MARRUBIUM VULGARE.

By Heber W. Youngken, Ph.D.

The writer recently secured a sample of a shipment labeled "horehound herb" that had been sent from a Greek port to a Philadelphia firm, but which was condemned by the government on the ground that it contained an adulterant. A cursory macroscopic examination failed to reveal the presence of any foreign leaf or stem, but critical observations showed it to contain a number of suspicious looking calyxes, much broader and more velvety in appearance than those common to *Marrubium vulgare*. He immediately set out to identify the foreign calyx, which presented characteristics of some *Ballota* species, and, after a lengthy search, came upon a single specimen in the herbarium of The Academy of Natural Sciences of Philadelphia, that was found identical with the calyx in question and which was labeled "*Ballota hirsuta* Benth." Upon looking up the characteristics of this species in Bentham's "Labiatarum Genera et Species," p. 595, he found the macroscopic aspects of the calyx identical. Through the courtesy of Professor Stewardson Brown, of the academy, he procured a leaf and calyx from a herbarium sheet, and these were studied comparatively with the foreign calyxes and fragments of leaves found in the sample. These agreed in every detail. Later the herbarium sheet of *Ballota hir-*

suta was borrowed and further macroscopic and microscopic details apprehended which proved conclusively that the adulterant was *Ballota hirsuta*. The characteristics of these two herbs and the important diagnostic differences are hereby presented.

FIG. 1.

FIG. 2.

FIG. 1. Aërial portion (to right) and branch (to left) of *Marrubium vulgare* L. $\times \frac{1}{3}$.

FIG. 2. Aërial foliage and floral stem of *Ballota hirsuta* Benth. Note the dense axillary clusters of flowers. $\times \frac{1}{3}$.

Marrubium vulgare Linnæus.

Marrubium vulgare L. (Fig. 1) commonly known as horehound, hoarhound, white hoarhound, or marvel, is a perennial herb indigenous to Europe and Central Asia. It is cultivated in various parts of the United States and has escaped in waste places throughout North America. The underground portion consists of a short rhizome bearing numerous slender rootlets. The aërial stem is erect, quadrangular, .3 to .8 M. high, 3 to 5 mm. in diameter,

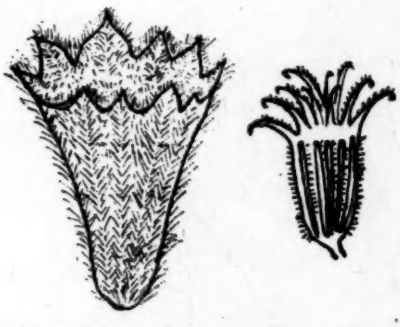

FIG. 3. Calyx of *Marrubium vulgare* to right; calyx of *Ballota hirsuta* to left. ×4.

branched, the branches ascending. Its white-wooly aspect is very striking. The leaves are opposite, petiolate, exstipulate, varying from ovate to broadly ovate to nearly orbicular in outline, 1.5 to 6 Cm. in length, 9 to 25 Mm. in breadth; apex obtuse; base narrowed or rounded or sub-cordate; margin coarsely crenate; upper surface downy-whitish, lower surface woolly; venation pinnate-reticulate. The infloresence is a verticillaster with flowers arranged in dense axillary whorls, each having a tubular sparsely pubescent calyx 6–7 Mm. long, with 10 subulate, recurved, bristle-like teeth (Fig. 3, *M*), a whitish bilabiate corolla, four parallel stamens ascending under the upper lid of the corolla, and a bi-carpellary pistil with a four-celled ovary. The fruit consists of four nutlets.

MICROSCOPIC CHARACTERISTICS OF *Marrubium vulgare* L.

The leaf shows the typical dorsoventral lamina common to the genus *Marrubium*. Transverse (Fig. 4) and surface sections show an upper epidermis, devoid of stomata, composed of tabular cells with somewhat undulate outer walls, a layer of vertically elongated

palisade cells, several layers of spongy parenchyma cells traversed by collateral bundles, and a lower epidermis similar to that of the upper, but possessing stomata. Non-glandular and glandular trichomes are present as outgrowths on both upper and lower epidermis. They are, however, more numerous on the lower epidermis. The non-glandular trichomes are either simple or branched,

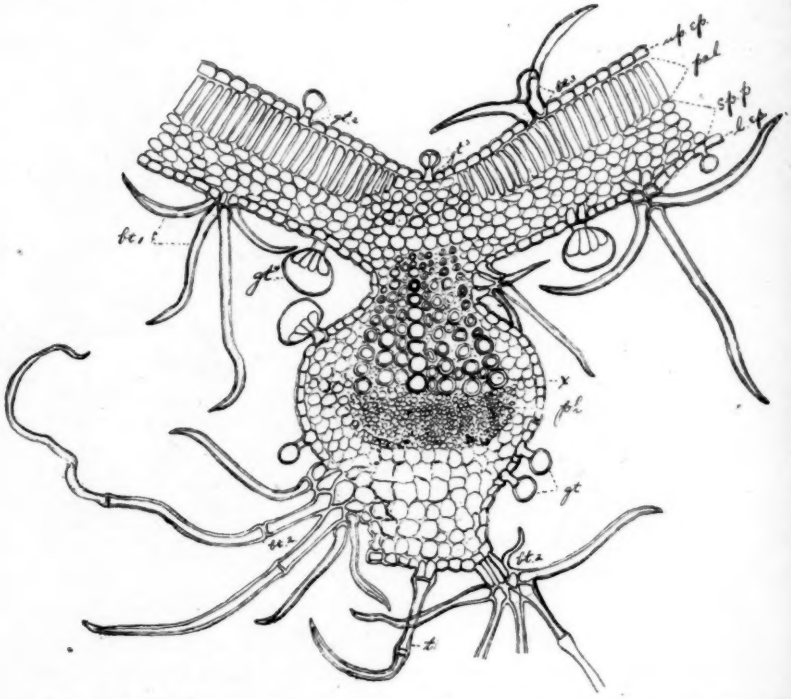

FIG. 4. Cross section through one of the stronger veins and portion of the lamina of *Marrubium vulgare*. *up. ep.*, upper epidermis; *l. ep.*, lower epidermis; *pal*, palisade parenchyma; *sp. p.*, spongy parenchyma; *x*, xylem; *ph.*, phloem; *t*, long-pointed non-glandular trichome; bt^1, bt^2, branched trichomes, more or less stalked; bt^3, sessile branched trichome; *gt*, gt^2, gt^3, gt^4, several types of glandular trichomes. × 120.

the latter type predominating. The simple trichomes are, for the most part, unicellular and almost invariably slightly curved. There occur, however, a scattering of much elongated, characteristically curved and twisted (in dried material) unicellular hairs which type predominate on the stem, giving this part its white-woolly aspect (Fig. 5, *J*). In addition to these, uniseriate two-celled hairs with the distal cell long-pointed and bent have been met with occasionally.

The branched trichomes are of two kinds, viz.: (1) those that project directly out of slightly elongated epidermal cells and which are two to three branched and (2) those which consist of a more or less elongated central multicellular stalk with radiating branches (Fig. 4). As many as fifteen branches have been observed on this type. Of these, those emanating from the base of the stalk are unicellular, and more frequently curved than straight, while those

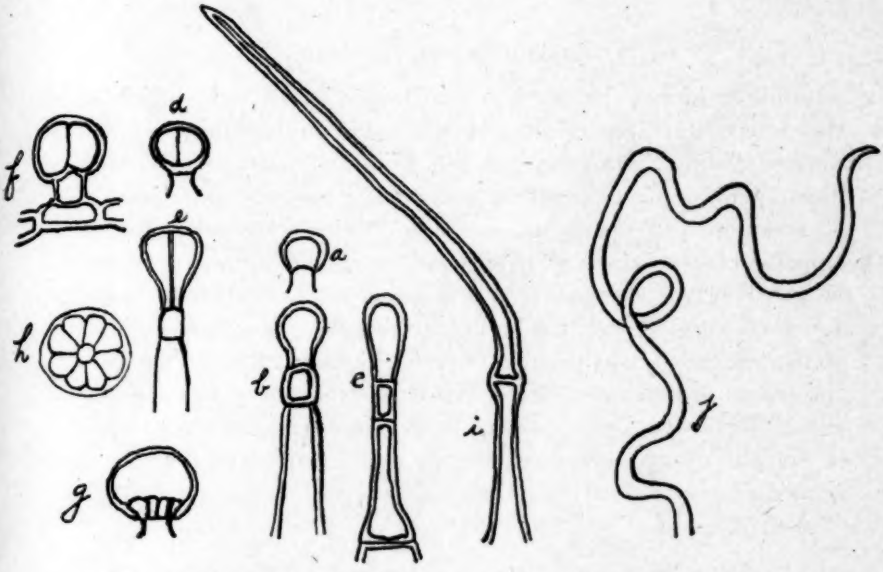

FIG. 5. Various types of hairs found on *Marrubium vulgare*. *a, b, c, d, e, f, g, h,* glandular hairs, and *i,* non-glandular two-celled hair, all found on the foliage leaves and calyxes; *j,* curled unicellular-non-glandular hair, a type abundantly found on the stem that gives to this part its white-woolly appearance. *a, d, f,* glandular hairs with a one-celled stalk and a one- to two-celled head; *b, c, e,* glandular hairs with two-celled uniseriate stalk and 1–2-celled head, the distal cell of the stalk being considerably shortened and forming the "neck cell"; *g,* side view, and *h,* view from above of large balloon-shaped glandular hair with one-celled stalk and 8-celled head. (All highly magnified.)

issuing from points higher up are either unicellular or two- or three-celled, the distal cell of these last being characteristically long, pointed and curved. The central stalk of the branched trichome does not usually attain the great length of the similar part of the branched trichome of *Ballota hirsuta*.

The glandular trichomes have either a one- to two-celled short or long stalk and a one-, two- or eight-celled balloon-shaped glandular head. The large number of the last mentioned (balloon) type which possess unicellular short stalks is very striking (Figs. 4 and 5).

Sections made through the calyx show to a modified degree the peculiar microscopic structure of the foliage leaf. The lamina is thinner and more trichomes of the glandular variety are evident.

Ballota hirsuta Bentham.

Ballota hirsuta Benth. is a perennial hirsute herb, which is indigenous to Mediterranean countries. The herbarium specimen examined (Fig. 2) presented the following macroscopic perculiarities: Stem quadrangular, pubescent but not white-woolly like *Marrubium.* Leaves, opposite, petiolate, ovate to orbicular, coarsely hairy on upper surface, coarsely whitish-woolly on under surface, apex obtuse, base sub-cordate, margin crenate, venation pinnate-reticulate. Inflorescence a verticillaster, the hermaphrodite flowers appearing in dense axillary clusters and usually fewer in number than in the verticillasters of *Marrubium.* Each flower consists of a bilabiate infundibuliform calyx, up to 10 Mm. long (Fig. 3, *B*) with limb showing a margin of 10 broadly acute or mucronate teeth, a distinctly bilabiate corolla, four included stamens, and a bi-carpellary pistil. The fruit consists of four nutlets.

Microscopical Characteristics of *Ballota hirsuta* Benth.

Transverse sections (Fig. 7) made through the lamina region of the foliage leaf show typical dorsoventral structure. Passing from ventral to dorsal surface the following structures present themselves for examination:

Upper epidermis, devoid of stomata and composed of tabular cells with outer walls more or less convex and showing a rather thick cuticle. Directly beneath this tissue is a layer of somewhat loosely arranged vertically elongated palisade cells, the average being shorter than those found in *Marrubium vulgare.* Beneath the palisade layer are several layers of more or less loosely arranged spongy parenchyma cells, irregular in shape. Through this region course numerous collateral fibro-vascular bundles marking the positions of the veins. The tracheæ of these have strongly lignified

walls, The most prominent peculiarities are shown by the trichomes which thickly cover both surfaces. These appear nearly equal in number as outgrowths of the epidermises. Both non-glandular and glandular types are represented. As for *Marrubium vulgare,* so for this leaf, the non-glandular trichomes fall into three categories,

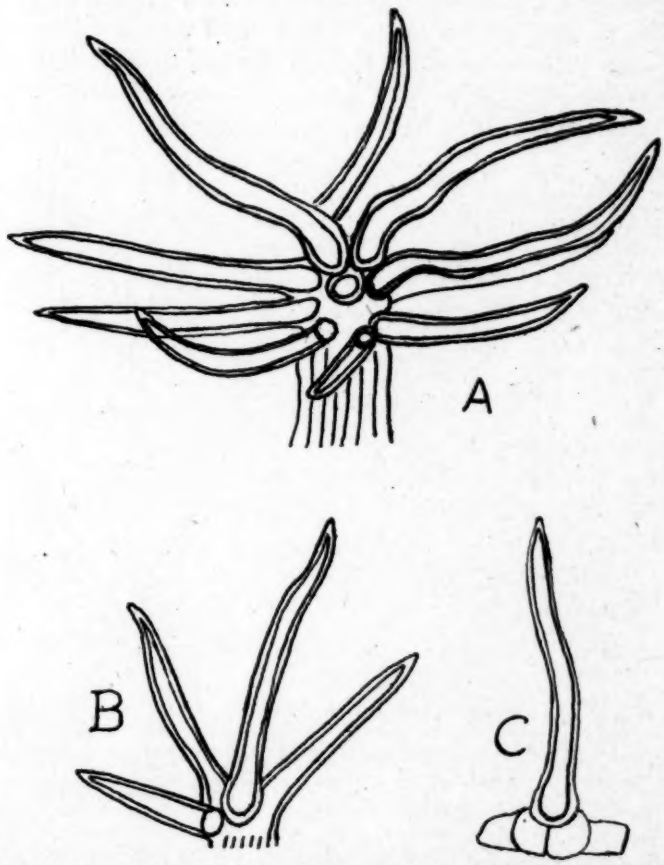

FIG. 6. Non-glandular hairs from calyx of *Marrubium vulgare. A,* many branched hair with somewhat elongated stalk; *B,* branched hair with short stalk and few branches; *C,* non-glandular unicellular hair. (All highly magnified.)

viz.: unicellular, uniseriate, and branched. The unicellular variety are either short or long, straight or bent over toward the epidermis. The individual cells of the uniseriate hairs form distinct articulations. By far the most conspicuous and diagnostic elements are the

branched hairs (Fig. 8). These are easily distinguished from those of *Marrubium vulgare* by their generally longer basal stalks, thicker walls and more rigid looking branches. As many as eighteen

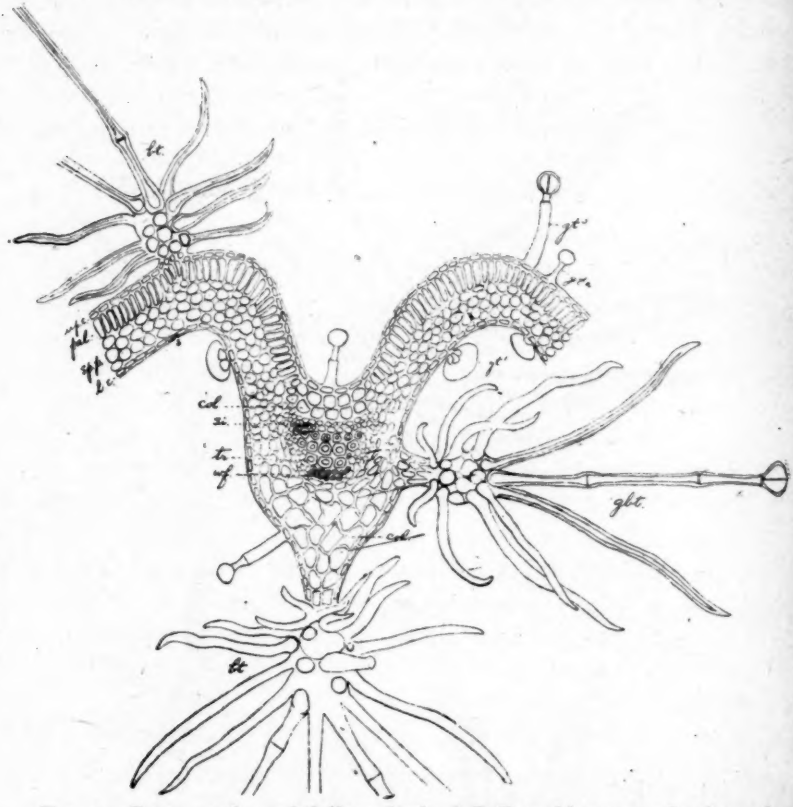

FIG. 7. Cross section of foliage leaf of *Ballota hirsuta* made through a stronger nerve and portion of the lamina. *up. e.*, upper epidermis; *l. e.*, lower epidermis; *pal.*, palisade parenchyma; *sp. p.*, spongy parenchyma; *s*, stoma; *col.*, collenchyma; *si.*, sieve tissue; *tr.*, trachea; *wf.*, wood fibers; *bt.*, branched trichomes; *gbt.*, branched trichome with central branch the longest and bearing a two-celled glandular head; gt^1, gt^2, gt^3, glandular trichomes. × 98.

branches have been counted emanating from the central stalk. The shortest branches arise from the basal portion, the rest becoming longer as the stalk is ascended. Most of the branches vary from one to three cells in length. The central or longest branch, however, may be uniseriate four-celled and attain a length of 3 Mm.

A form of branched trichome has been observed by the writer that stands out preëminently as constituting the most easy and practical histologic means of distinguishing *Ballota hirsuta* from *Marrubium vulgare*. This trichome resembles the other branched forms seen in *Ballota* but differs from these is respect to the central branch which has a two-four celled uniseriate stalk and a glandular head of one or two to four cells (Fig. 8, *A*).

The glandular trichomes exhibit various forms (Fig. 9) viz.: (*a*) short one-celled stalk and small unicellular head; (*b*) short unicellular stalk and large four to eight-celled balloon-shaped head; (*c*)

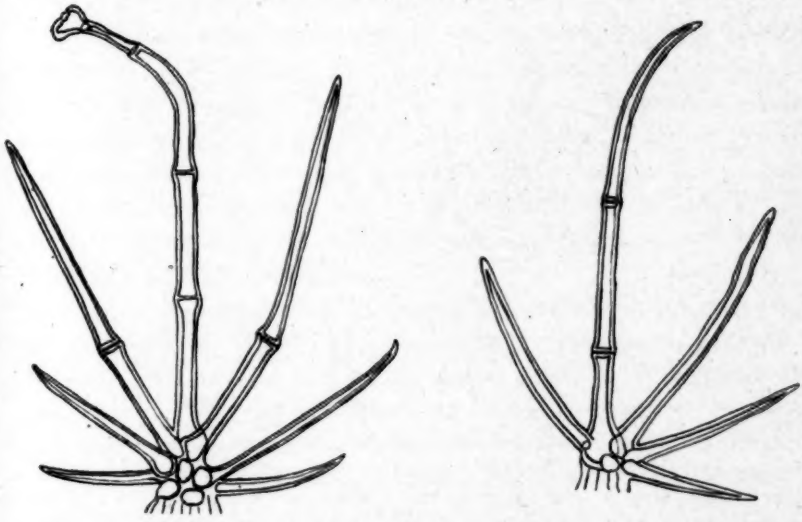

FIG. 8. Types of branched hairs found on the foliage leaves and calyxes of *Ballota hirsuta*. The illustration to the left shows one of these, the central branch of which is longer than the rest and bears a glandular head at its summit. (Highly magnified.)

long one-celled stalk and small spheroidal unicellular head; (*d*) long one-celled stalk and elongated unicellular head; (*e*) one-celled stalk and two-celled head; (*f*) short two-celled stalk and two-celled head; (*g*) long two-celled stalk, the distal cell ("neck cell") being shorter than the proximal one and bearing a one-celled head. Many of the hairs have their basal portions lignified. These take a pinkish to reddish coloration with phloroglucin and concentrated hydrochloric acid.

The calyx of *Ballota hirsuta* shows a microscopic structure simi-

lar to that of the foliage leaf, but on a reduced scale. The tendency for more of the branched hairs to show the central branch glandular has been observed.

The chief practical diagnostic differences between *Ballota hirsuta* and *Marrubium vulgare* are as follows:

1. The calyx, which in *Ballota hirsuta* is densely hairy, distinctly bi-labiate-infundibuliform with limb margin showing 10 broadly acute or mucronate teeth, whereas in *Marrubium vulgare* it is sparsely hairy, distinctly tubular with ten bristle-like recurved teeth.

2. The absence in *Marrubium vulgare* and presence in *Ballota hirsuta* of certain branched trichomes, the central branch of which bears a glandular head or one of two to four cells.

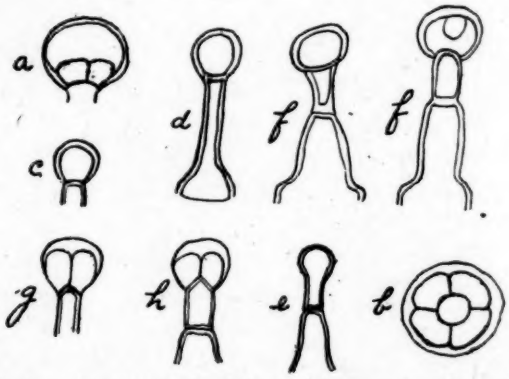

FIG. 9. Various types of glandular trichomes found on the calyx and foliage leaf of *Ballota hirsuta*. *a*, lateral view, and *b*, view from above of the balloon type of glandular trichome showing (in *a*) a short unicellular stalk and (in *b*) a four-celled glandular head; *c*, *d*, *e*, *f*, *g*, other types of glandular hairs having a 1–2-celled stalk and a 1–2-celled glandular head. (All highly magnified.)

3. The branched trichomes of *Ballota hirsuta* show on the average longer basal stalks, thicker walls and more rigid branches than those of *Marrubium vulgare*.

4. A number of trichomes of *Ballota hirsuta* are lignified at their bases, whereas in *Marrubium vulgare* no such lignification has been observed.

PHARMACOGNOSY RESEARCH LABORATORY,
PHILADELPHIA COLLEGE OF PHARMACY.

LITERATURE.

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A REVIEW OF THE ADVANCES IN PHARMACY.

By John K. Thum, Ph.M.,

LANKENAU HOSPITAL, PHILADELPHIA.

The Potash Situation.—In 1914, the United States Geological Survey and the Bureau of Soils were given funds to undertake an investigation as to the possibility of developing the potash industry in this country. This investigation has proven of considerable value and the results are the beginning of what will eventually prove to develop into a great American industry.

Since 1914 wonderful progress has been made. Only recently Secretary Lane optimistically declared that within two years this country will be independent of outside sources of potash. What this means may be readily imagined from the fact that our pre-war demands and necessities for this important substance amounted to well over 1,000,000 tons, nearly all of which was imported. The question of an adequate potash supply is a vital one, and of far-reaching economic importance.

One of the first sources of this substance to be investigated was the vast deposit of kelp along the Pacific coast from Mexico to Alaska. At first the kelp was merely dried or incinerated and ground to powder. It was afterward found that it could be handled in a more profitable manner which would result in the production of other valuable chemicals, with potash relegated to the position of a by-product. As an example, the Hercules Powder Company at San Diego, California, has built a large plant where the kelp is not dried, but fermented, yielding not only potash, but acetone, iodine and other products, including algin, which it is predicted may ultimately become commercially valuable.

Investigation has revealed another source of potash in the United States and that is the flue of blast furnaces and the dust of cement kilns. The production of potash from this source requires a rather highly technical operation, and is mainly carried out by means of an apparatus known as the Cottrell electrical precipitator, in which the potash is separated out and collected by electrostatic precipitation. Many iron ores, especially those of Alabama, contain about three per cent. of potash, most of which is recoverable. It is esti-

mated that if all the blast furnaces in the United States installed this process, nearly 1,000,000 tons of potash could be obtained from this source alone. From the cement works, where the potash is collected in the same manner, the Bureau of Soils estimated from investigations carried out, that the cement kilns could, in the aggregate, yield nearly 100,000 tons of potash each year.

Another source of potash in this country is the salt lakes, which are particularly interesting and seem to promise great things in the way of making this country independent of other countries for our potash. One of these wonderful lakes—Searles Lake, in California—consists of a vast mass of salt crystals about twelve square miles in area and seventy feet deep, all the water having evaporated. A bulletin issued by the United States Geological Survey, makes the statement that the main central salt deposit is a firm and very porous bed of salt crystals; indeed it is so firm and hard that roads are made on it, and it is no uncommon thing for teams and motor trucks to drive over its surface, and even the concrete foundations of the American Trona Corporation's pump house were laid on the surface. The average potash content is four per cent. in the form of the chloride. This corporation is producing about 4,500 tons of crude potash salts per month, and is also turning out about 50 tons of borax per day.

Other sources of potash which are looked upon as promising are the mineral silicates, such as feldspar, sericite, and alunite. In Marysville, in southern Utah, the Mineral Products Corporation has already put up a plant with an output at present of about 600 tons per month of sulphate of potash. There are signs that aluminum as well as potash will ultimately be obtainable from these minerals: indeed, it is predicted by some investigators that this may prove a better course of aluminum than bauxite. With all these sources of supply for this very necessary substance let us hope that prices will soon drop to reasonable proportions.[1]

Quinine-Formaldehyde Solution in War Surgery.—The advantages claimed for this solution are that it is easily prepared, is stable, can be readily concentrated for transportation, the strength can be easily increased or diminished, and it can be used in an early stage of wound treatment, at the field or evacuation hospital. The formula for the solution is as follows:

[1] *The Living Age*, vol. 13, 1919, 183.

Quinine sulphate	1.00 gm.
Acid hydrochloric	0.50 mils
Acid acetic (99 per cent.)	5.00 mils
Sodium chloride	17.50 gms.
Liquor formaldehyde, U. S. P.	1.00 mil
Thymol	0.25 gm.
Alcohol (90 per cent.)	15.00 mils
Distilled water	q. s. 1,000.00 mils

Dissolve the quinine in the acids; dissolve the sodium chloride in the water; dissolve the thymol in the alcohol; mix the first two solutions and add to this mixture the formaldehyde solution, and then to the combined solutions add the thymol solution.

The technic for the application of this solution is similar to that used in the treatment of wounds by the Carrel-Dakin solution, or it may be injected through the Carrel tubes every two hours, or more frequently, if necessary, to keep the wound bathed with it.

Its efficacy was pretty well tried out in a series of 100 badly infected wounds at the American Red Cross Military Hospital No. 5, many of which were compound comminuted fractures, which had been treated for from ten days to two weeks or longer with Dakin's solution, and in which the bacterial flora showed no signs of decrease in the great majority of cases. There was a marked drop in temperature and pulse in many cases on changing from Dakin's to quinine-formaldehyde solution, without any operative procedure. Some wounds showing a count of 10 to 15 bacteria per field apparently have been rendered free from germs within three days. That is to say, none have been found in the repeated examination of fifteen fields Thirty consecutive cases treated within thirty-six to forty-eight hours after receipt of injury, on whom preoperative smears were made and the presence of infection established, were rendered sterile within forty-eight hours and have continued to show absence of any bacteria on repeated counts subsequently, with one exception.—*Annals of Surgery,* Philadelphia, vol. 68, 1918, 467.

Feeding Experiments with Raw and Boiled Carrots.—Any contribution that will add to our present scanty knowledge of vitamins is surely worth-while recording. Denton and Kohman feel that in the present food crisis a knowledge of the dietetic properties of root vegetables is of prime importance, and especially so since the use of dehydrated vegetables promises to come into general vogue. In their experiments they found that carrots, when properly reinforced

with starch, casein, butter or lard, and salts, to such an extent that 50 per cent. of the caloric value of the diet is silll derived from the carrots, will produce normal growth and reproduction in albino rats. Carrots as an exclusive diet, except for the addition of chlorine, calcium, phosphorus, sodium, may support animals in apparently good health for as long as sixteen weeks. The animals on such a diet maintain and very often increase their body weight. It was demonstrated that carrots contain an unusually large amount of both the water-soluble and fat-soluble vitamins. They believe that ordinary methods of cooking do not materially injure the nutritive value of carrots, certainly not when used as part of a mixed diet. They are convinced that a considerable portion of the caloric value of the food is lost when the water used in cooking is rejected.—*Jour. Biological Chemistry,* Baltimore, vol. 36, 1918, 249.

Determination of Citral.—According to Parker and Hiltner in making determinations for citral by the latter's colorimetric method with metaphenylenediamine hydrochloride it will happen at times that lemon and orange oils and extracts give blue or green colors in place of yellow, which makes the use of this method more or less restricted. Investigation showed that this was due to oxidation of some constituent of the citrus oil, and experiments tended to show that the addition of a certain amount of oxalic acid to the original Hiltner reagent would be a most practical way of preventing such blue coloration. The reagent as modified by them is made by dissolving 1 gram of the metaphenylenediamine hydrochloride and 1 gram of crystallized oxalic acid, each in 45 mils of 80 per cent. alcohol; the two solutions are then mixed and the volume brought up to 100 mils with 80 per cent. alcohol. This solution is then shaken up with three grams of fuller's earth and filtered. They give detailed information as to the use of this colorimetric method and the necessary calculations.—*J. Ind. and Eng. Chem.,* vol. 10, 1918, 608, through *The Analyst,* Nov., 1918.

The Output of Platinum.—In conjunction with the usual uses to which this valuable metal is put, namely electrical appliances, crucibles, etc., the requirements were greatly augmented during the war on account of the increased needs for internal combustion engines for airplanes, automobiles, tanks and motor boats, the manufacture of fuming sulphuric acid, for which the metal is em-

ployed as a catalyzer, the acid being one of the prime needs in the making of munitions, and in the fixing of nitrogen from the air, which in turn is used for manufacture of explosives. Before the war 90 per cent. of the world's output of this mental was produced from Russia. The Russian and the newer and less developed field in Colombia, South America, comprise the world's two important sources of the valuable metal. In spite of the great demand for this metal in carrying out important manufactures engendered by the war, the production in Russia fell from 300,000 ounces in 1911, to about 78,000 ounces in 1916. However, to sort of counteract this decrease in production from this source, production in the Choco district of Columbia increased from 12,000 ounces in 1911 to nearly 50,000 troy ounces in 1917, which is an increase of 300 per cent in this practically new field. It undoubtedly will be a source of satisfaction to American manufacturers who need this metal to know that they have easy access to this promising field instead of depending on far-off chaotic Russia.—*Jour. Amer. Med. Assoc.*, vol., 72, 1919, 411.

Narcotic Drug Control.—The new law dealing with this important matter in the state of New York became effective on February 1. Plans for its enforcement have been formulated which authorize representatives to visit all persons or institutions having authority to possess, dispense or prescribe habit-forming drugs to ascertain if their records comply with the law, and in case of violation to bring the offender to account. In a communication to the New York County Medical Society the commission having charge of the enforcement of the law make clear that it realizes that many of the problems are administrative, educational and medical rather than legislative, as was shown by the testimony brought out at the hearings of the legislative investigating committee. Therefore the commission desired to so administer the law as to hamper the honest physician as little as possible. It was also announced that it would be the commission's purpose to so administer the law that those unfortunates, the drug addicts, will be cared for and safeguarded against the growing evil. This commission evidences a desire for the coöperation and assistance of all the medical organizations of the state in controling and eventually eradicating this pernicious evil and doing away with abuses practised by some of those legally entitled to possess and dispense drugs of this kind.—*Jour. A. M. A.*, vol. 72, 1919, 431.

Idiosyncrasies to Drugs.—Civalleri comments on the fact that the term medicinal anaphylaxis is coming to be used instead of the old term idiosyncrasy. He discusses the literature on the subject, especially that in which quinine is involved. Among other instances, he makes note of a case mentioned by Pereira in which a second injection of quinine, given fifteen years after the first injection, gave rise to a train of grave symptoms that could only be explained as anaphylactoid phenomena in a previously sensitized individual. Civalleri confirmed this experience of Pereira's by experiments of his own on guinea-pigs. Serious and sometimes fatal phenomena were induced almost constantly by parenteral injections of quinine in previously sensitized animals in doses which normal guinea-pigs tolerated perfectly. Effects were most pronounced with intervals of from three to twenty days. The smallest sensitizing dose, by the peritoneum, was 0.04 gram. As quinine cannot be said to be an antigen, and as there is no production of antibodies with it, the reaction cannot be called a true anaphylaxis, although it is closely analogous. Civalleri would describe it as an allergy to a non-antigenic substance; he says that it may be acquired or congenital or inherited. —*Rivista Critica di Clinica Medica,* Florence, vol. 19, 1918, 421.

Preliminary Report of Method for Estimating in Vivo Germicidal Activity of Antiseptics.—With the idea of reducing the margin of error in estimating the bacterial contents of a wound with microbe charts Perkins and his associates have been culturing the wounds, counting the number of colonies and plotting curves as in microbe charts. To reduce the element of personal equation the work has been done by one man. Inoculations were made from the same part of the surface of the wound, one definite spot being selected and used throughout; the same platinum wire loop was used each time in an endeavor to get a uniform sized drop. The drop obtained was inoculated at the bed-side in 2 mils of plain bouillon, the bouillon suspension, undiluted, was immediately poured over an agar-agar plate, which was then covered and turned upside down and marked with the patient's number, the number of the culture, and the time the culture was taken. The plate was then taken to the laboratory and placed in an incubator and kept at 37° C. At the end of twenty-four hours the colonies were counted, macroscopically, and recorded. Carrying out this procedure during different stages of wound treatment with antiseptics some idea can be

obtained of the comparative strength of antiseptics and the length of time during which they are active when applied to human tissues in the presence of infection.—*Annals of Surgery,* Philadelphia, vol. 3. 1918, 68.

Carbon Tetrachloride Vapor as a Delousing Agent.—Dr. Foster, of the United States Public Health Service, gives out a preliminary report on experiments for the destruction of lice in clothing by the vapor of carbon tetrachloride. Heat and hydrocyanic gas are undoubtedly the best agents for this purpose, but require a rather complicated apparatus for their use and can be used to advantage only where the work is to be done on a large scale. The experiments were undertaken to find some agent that could be used anywhere and for small operations. Carbon tetrachloride vapor was found to be effective after two hours exposure with the clothing rather closely packed in a tin or other vessel that is air-tight, in an amount of 25 mils. The clothing to be disinfected should not occupy more than half or two thirds of the containing vessel. In these experiments only the lice were killed. The nits were only partly killed, but their hatching was delayed. The method evolved was simple; the material was packed in the can, on top of which was placed several layers of filter paper, on which was poured the carbon tetrachloride. The can was then covered with several thicknesses of toweling and a loose cover placed over this. In some experiments, the lice-infested material was wrapped tightly in papers; various combinations of carbon tetrachloride with gasoline were also tried out. It was found, however, that unadulterated carbon tetrachloride was more effective and the lice were always killed in about the time mentioned. At the present price of carbon tetrachloride, the cost for treatment of the clothing of a single soldier will amount to from one and a half to five cents.—Public Health Reports, October 25, 1918.

EXAMINATION OF A SAMPLE OF GUM ASAFŒTIDA.

By Edo Claassen,

East Cleveland, Ohio.

A piece of gum asafœtida, in which whitish, shining specks could be seen, was subjected to an examination to determine its purity. It weighed 9.310 Gm. By extracting it with hot water, followed by some alcohol, it left a residue, composed of particles of rock, partly whitish and shining, partly grayish with black spots. The first proved to be calcite and the others granite, the black spots in this being amphibole; their weight was 4.241 Gm. The granite particles, one of which weighed 0.820 Gm., could be easily separated by a pair of pincers; they weighed 0.935 Gm., so that the calcite amounted to 3.306 Gm. It will be seen that the adulterations represented nearly half the quantity of the gum, the percentage being gum 54.45 per cent., calcite 35.51 per cent. and granite 10.04 per cent.

The adulteration of another piece of gum, previously examined, consisted of calcite only in about the same amount.

A NOTE ON CRYSTALLIZED GALL STONES.

By Edo Claassen,

East Cleveland, Ohio.

Quite a number of interesting bodies were passed by a woman, 45 years old. Most of them were small, grainlike; several, however, were of a larger size, up to that of a pea. Their color was yellowish, somewhat shining. Heated on platinum foil, they melted at first, then evaporated, leaving a little of a dark substance and when ignited, burned with a yellow flame. They dissolved in hot alcohol, the solution leaving, when evaporated on a slide, four-sided rhombic plates; the largest crystals, being polyhedral with a diameter from 6 to 10 millimeters and weighing up to 0.384 Gm. One of these, particularly, weighing 0.208 Gm., surpassed the others by its quite regular shape; it belonged to the regular (the tesseral) crystal system, being a combination of the predominant cube with the octahedron and the dodecahedron = ∞ O ∞·O·∞ O., which was proven by measuring its angles by means of a hand goniometer. All the above properties are known to be such, as belong to cholesterin, which in fact they represent.

IS IT WORTH WHILE?[1]

" I was having a long talk to one of my colleagues last night, and we were discussing how doubtful we felt as to whether it was worth while continuing to take an active interest in pharmaceutical affairs. The opinion we came to was that it was a matter of individual temperament. My own opinion is that there can be no half measures. 'Taking an interest' means giving up time, energy, recreation, and even cash. Unless a man is prepared to work on these lines, he had better resign and be done with it.

" Yours, feeling rather stale,

" X. Y. Z."

The above letter reached us a few days ago from one of the leaders of Australian pharmacy. It typifies in a general way the feeling that every man who takes an interest in public affairs experiences at some time or other during his career. Despondency as to practical results achieved by his efforts, annoyance at the indifference and lack of appreciation of the rank and file, and irritation because of the conservatism of some, and the disloyalty of others are factors which invariably lead to the heart-searching question: " Is it worth while? "

The ethics of voluntary service presupposes a willingness to make personal sacrifices. There are compensations, it is true, but these cannot always be tangibly expressed. The hope of reward is not always present to sweeten the labor. Each man knows his own duty best. To some the call to public service is insistent. Every individual more or less possesses some of the characteristics which make for good citizenship. In pharmacy in particular the craft has never lacked men of foresight and character as its leaders. Today quite as much as in the past the need for leadership of the right sort exists. The best minds of all engaged in the craft should be available, and in no sense are they too good to be utilized for the advancement of the cause which every true pharmacist has at heart. But it should not be overlooked that in addition to those excellent qualities already mentioned, patience, persistence, and perseverance are equally important. Time is always on the side of the reformer. Often the steady plodder accomplishes more in the long run than his more brilliant and scholarly colleague. Few reforms

[1] Reprinted from *The Australian Jour. of Phar.*, November 18.

are gained without long periods of preparation. Pharmaceutical history amply illustrates this. How much pharmacists to-day owe to the early pioneers for years of faithful service is hard to say. Their deeds live after them, and we know that their memory is both cherished and honored.

Edmund Burke in "Thoughts on the Cause of Present Discontents" says that "The man who lives wholly detached from others must be either an angel or a devil. . . . We are born only to be men. We shall do enough if we form ourselves to be good ones. It is therefore our business carefully to cultivate in our minds every sort of generous and honest feeling that belongs to our nature. To model our principles to our duty and our situation . . . and rather to run the risk of falling into faults in a course which leads us to act with effect and energy, than to loiter out our days without blame, without use. Public life is a situation of power and energy; he trespasses against his duty who sleeps upon his watch as well as he that goes over to the enemy."

Burke's eloquence might well act as a guide and stimulus to those who are inclined to falter in their work. The call to service is insistent in the hearts of men. Whether little or much results from their efforts depends to a great extent upon the amount of enthusiasm and energy they give out themselves and inspire in others. No one can truthfully say that service of this kind faithfully rendered is not worth while. It would be a thousand pities if because of some temporary discouragement there should be any diminution in the ranks of those to whom pharmaceutical service means not merely a perfunctory duty or drudgery, but an exemplification of good citizenship in the performance of which all that is best in them finds truthful expression.

A NEW METHOD FOR THE DETERMINATION OF VANILLIN IN VANILLA EXTRACT.[1]

By Arthur W. Dox and G. P. Plaisance,

Chemistry Section, Iowa Agricultural Experiment Station.

The official method for the determination of vanillin in vanilla extract consists essentially in removing the alcohol, extracting the vanillin with ether, crystallizing it from the ethereal solution and weighing it directly, identifying the crystals if necessary by their melting point. This method was first proposed by Hess and Prescott.[2]

Modifications were subsequently introduced by Winton and Silverman,[3] and by Winton and Bailey.[4]

For details of manipulation reference should be made to the official methods of the A. O. A. C.[5]

The whole operation is rather lengthy and tedious.

Methods dependent upon the precipitation of vanillin by various reagents have been suggested but have not come into common use. Hanus[6] used m-nitrobenzoylhydrazide as a precipitant, and also platinic chloride[7] for estimating vanillin in the presence of piperonal. Moulin[8] converted the vanillin into a yellow methyl picrate and estimated it colorimetrically. More recently Folin and Denis[9] have devised a colorimetric method based upon the color obtained by means of phosphotungstic and phosphomolybdic acids.

The writers[10] have found that thiobarbituric acid in the presence of 12 per cent. hydrochloric acid is a general reagent for the precipitation of aromatic aldehydes and have applied it to the quantitative determination of furfural[11] Under these conditions vanillin gave with thiobarbituric acid an insoluble vermillion colored pre-

[1] Reprinted from *Simmons' Spice Mill,* November, 1918.
[2] *J. Am. Chem. Soc.,* 21, 256 and 719, 1899.
[3] *Ibid.,* 24, 1128, 1902.
[4] *Ibid.,* 27, 719, 1905.
[5] Bur. Chem. Bull. No. 152, p. 146.
[6] *Zeitschr. Untes. Nahr. Genussm.,* 10, 585, 1905.
[7] *Ibid.,* 10, 657, 1900.
[8] *Bull. Soc. Chem.,* 29, 278, 1903.
[9] *J. Ind. Eng. Chem.,* 4, 670, 1912.
[10] Dox and Plaisance, *J. Am. Chem. Soc.,* 38, 2164, 1916.
[11] Dox and Plaisance, *ibid.,* 38, 2156, 1916.

cipitate, which analysis showed to contain the percentages of nitrogen and sulphur required for the simple condensation product, 3-methoxy-4-hydroxybenzalmalonylthiourea. Since the reaction appeared to be practically quantitative, we decided to test out its possible application as a means of quantitatively estimating vanillin.

The first experiments were conducted with a standard solution of pure vanillin. Aliquots of this solution were precipiated with thiobarbituric acid in the presence of 12 per cent. hydrochloric acid. The total volume of the reaction mixture was 50 Cc. The precipitates were allowed to stand over night, then filtered on Gooch crucibles, washed with 50 Cc. 12 per cent. hydrochloric acid in small portions and finally with 20 Cc. of water. The results are set forth in the following table:

Van. Taken, G.	Weight of Precip , G.	Van. Recov.	Error, Mg.
.0200	.0330	.0180	−2.0
.0200	.0337	.0184	−1.6
.0200	.0336	.0184	−1.6
.0200	.0330	.0180	−2.0
.0500	.0877	.0480	−2.0
.0500	.0890	.0487	−1.3
.0500	.0885	.0484	−1.6
.0500	.0890	.0487	−1.3
.0500	.0888	.0486	−1.4
.0500	.0906	.0496	−0.5
.0500	.0900	.0492	−0.8
.0500*	.0890	.0487	−1.3
.0500*	.0890	.0487	−1.3

In each case the filtrate was a lemon-yellow color, indicating that a small amount of the condensation product remained in solution. This observation is furter substantiated by the fact that the vanillin recovered is somewhat less than the amount taken. The error is, however, quite uniform, regardless of the amount of vanillin taken, averaging 2.6 Mg. of the condensation product or 1.4 Mg. vanillin. It is apparent therefore that a solubility correction must be applied just as in the determination of furfural by the official phloroglucinol method.

Before applying the method to the determination of vanillin in commercial vanillin extracts, where clarification is necessary, the use of lead acetate as a clarifying agent was tested. In the last two determinations in the above table, lead acetate was added and the

* Clarified with lead acetate.

excess removed from the filtrate by hydrochloric acid before adding thiobarbituric acid. The results are in close agreement with the other results, showing that the small amount of lead chloride remaining in solution does not interfere with the determination.

A sample of vanilla extract of known purity was next used. The procedure was as follows:—25 Cc. of the extract were dealcoholized in the usual manner, then transferred to a 50 Cc. standard sugar flask and filled to the mark with lead acetate solution. After standing for several hours at about 37° C. the contents of the flask were filtered through a dry filter. The filtrate was a straw color, indicating the absence of caramel as added coloring matter. 40 Cc. of this filtrate was then transferred to another 50 Cc. flask. Sufficient concentrated hydrochloric acid was added to bring the volume to 50 Cc. and the acidity to 12 per cent. After standing a few minutes the lead chloride was removed by filtration through a dry filter and 40 Cc. of the filtrate taken for the determination. On adding thiobarbituric acid in 12 per cent. hydrochloric acid solution, an orange-colored precipitate resulted, indistinguishable in color from the product with pure vanillin. However, the color of the filtrate was somewhat darker than with vanillin alone, due no doubt to the original color of the filtrate after clarification. The precipitate was allowed to stand over night filtered on a Gooch crucible, washed with hydrochloric acid and water as in the previous determination and dried at 98°. The results were as follows:

Vanilla Extract Taken, Cc.	Aliquot Per Cent. of Extract Taken.	Wt. of Precipitate, G.	Wt. of Precipitate Corrected for Solubility.	Vanillin found in Aliquot.	Vanillin in 25 Cc. Extract, G.	Vanillin in Extract Per Cent.
25	64	.0450	.0476	.0260	.0406	0.16
25	64	.0450	.0476	.0260	.0406	0.16
25	72	.0501	.0527	.0288	.0400	0.16
25	72	.0498	.0523	.0286	.0397	0.16
25	72	.0510	.0536	.0293	.0407	0.16
25	72	.0501	.0527	.0288	.0400	0.16
25	72	.0502	.0528	.0289	.0401	0.16
25+	80	.0890	.0916	.0501	.0626	0.25
25+	80	.0882	.0908	.0496	.0621	0.25

The above method is not applicable to artificial extracts where caramel is added as a coloring matter, since caramel contains furfural derivatives which react with thiobarbituric acid. The absence of caramel should first be demonstrated qualitatively. When caramel is present, the filtrate after clarification is brown instead of

straw-colored. A still more delicate test, described here for the first time, is the reaction with phloroglucinol. After clarifying and removing the excess of lead as chloride, phloroglucinol is added. In the presence of caramel a brown precipitate is formed. If caramel is absent, the vanillin gives a delicate rose-pink color or a slight pink precipitate. Clarification of the sample is necessary, as shown by the fact that the two determinations without clarification gave high results.

SUMMARY.

Thiobarbituric acid, which is easily prepared from malonic ester and thiourea, may be used for the quantitative determination of vanillin in vanilla extracts which do not contain caramel as added coloring matter. When caramel is present it may easily be detected by the brown precipitate formed on the addition of phloroglucinol to the clarified extract containing 12 per cent. hydrochloric acid.

CHLORAMINE REACTIONS OF PROTEINS.[1]

BY J. F. BRIGGS.

The attention which has been paid to the use of hypochlorous acid in antiseptic surgery in recent times has indicated the necessity for a clear expostiion of the chemical functions of the chloramines generally and of the chloramine derivatives of the proteins in particular. A complete discussion of the clinical aspect of the subject recently appeared in a paper read before this society by Dr. T. Rettie,[2] and reference may also be made to publications by Dakin and others.[3] The object of the present note is to recall attention to the important researches of Raschig,[4] in which the reactions of the chloramine group were outlined, and a process for the preparation of hydrazine by means of these reactions was established. About the same time, Cross, Bevan and Briggs[5] found in Raschig's results the explanation of certain hitherto obscure facts in connection with flax bleaching, and indicated the future importance of this general

[1] Reprinted from *Journal of Society of Chemical Industry*, December, 1918.
[2] *Ibid.*, 1918, 23 T.
[3] *Ibid.*, 1915, 919, 977; 1916, 651.
[4] *Ber.*, 1907, 40, 4586; *Chem.-Zeit.*, 1907, 31, 926.
[5] *Ibid.*, 1908, 261.

reactivity of the amino group. As an industrial operation the chlorination of wool had long been known, and the physical modification produced by the treatment utilized, but the persistence of the active chlorine in the treated protein was considered more or less as a technical perversity rather than a fundamental consequence of the reaction.

Our investigation of this wide subject did not pretend to be exhaustive, and many "loose ends" were left both in the qualitative and quantitative aspects of the subject. Raschig's original work related only to the monochloramine group, NH_2Cl, or in the case of organic amino compounds RNHCl, and the circumstances under which the second hydrogen atom is replaceable by halogen were left undecided. This uncertainty, coupled with the susceptibility of the products to progressive decomposition, led to the failure which we subsequently encountered in our attempts to establish an easy iodometric method for the estimation of amino nitrogen in solution, after removing the excess of hypochlorite by hydrogen peroxide and the excess of the latter by shaking with black manganese dioxide. Positive results were obtained for a large variety of compounds, but their variation with the time and temperature factors caused us to abandon hope of producing a workable analytical process.

All kinds of protein derivatives give the chloramine reaction regardless of their state of complexity and solubility. Thus, complex protein colloids like silk and wool combine with the halogen without entering into solution, gelatin in aqueous solution is percipitated in the form of an insoluble chloramine, peptones, albumoses and simple amino derivatives give chloramine compounds which are soluble in their respective degrees. This wide range through all grades of colloids and colloidal solutions to crystalloids explains the observation that at certain stages colloidal chloramines may be absorbed from old bleaching liquors by vegetable fibers. Certain observations made in those early days are worth recalling in view of the physiological interests which this group of compounds has attained. It was suggested at that time that the persistent odor which clings to the hands after immersion in hypochlorite solutions was due to protein chloramine, and this suggestion appears to have been fully corroborated. Other cases of "chemical" odors developed in bleached fabrics have been traced to a similar cause.

In the recent clinical publications great stress has been laid on the alkalinity of hypochlorite solutions and on the necessity of

counteracting this alkalinity by the addition of a weak acid. It must, however, be pointed out that part of this reputed alkalinity of the hypochlorite solution may really be the result of the chloramine reaction. It is certainly the case that a solution of sodium hypochlorite adjusted to complete neutrality by titration still feels strongly "caustic" to the hands. This is explained by reference to the original reaction $RNH_2 + NaOCl = RNHCl + NaOH$. Whenever a chloramine is formed from a neutral hypochlorite, caustic alkali is liberated, and it would be interesting to ascertain whether this equation is capable of affording a volumetric analytical method. Alkali acts to a certain extent as a stabilizing agent on the chloramines, and, on the other hand, when a neutral chloramine decomposes, hydrochloric acid is liberated according to the reaction $3RNHCl = N_2 + RNH_2 + 3HCl$. From these two equations the advantage in surgical work of the addition of a polybasic acid, such as boric acid, capable of giving amphoteric salts, becomes very obvious.

In our technical investigations we paid special attention to the chloramine reactions of gelatin as typical of the group, depositing it on cotton yarn as an aqueous solution, and fixing it in the form of insoluble chloramine. This treated yarn, after thorough washing, still retained the active chlorine reaction. Previous combination with formaldehyde did not affect the normal course of the reaction. If a cake of dry gelatin is steeped in a hypochlorite solution for several hours the outside is converted into a hard layer of insoluble chloramine, but the gelatin swells in the ordinary manner. If it be then washed and transferred to hot water, the gelatin of the interior dissolves and is liberated by puncturing the outer skin, leaving an empty bag of gelatin chloramine. It is possible that this phenomenon might be utilized in diffusion experiments, and the chloramine membrane might exhibit special semipermeable effects. When the gelatin chloramine is dried in the oven it is decomposed with the evolution of gas and development of free hydrochloric acid.

As a qualitative test for localized deposits of proteins the chloramine reaction is unexcelled. Stains of protein fluids on fabrics, the presence of wool fibers in cotton, the presence of glue or casein in adhesives and coatings, are easily demonstrated by chlorinating, washing, and developing the color reaction with potassium iodide and starch. The most minute fragment of the sample will suffice for the test, and in special cases the original sample of fabric may

be restored uninjured by treating with an "antichlor" after performing the test. The localization of protein in plant tissues can be demonstrated in the same way by the treatment of their sections; for instance, a thin slice of potato shows a very beautiful network.

Enough has been said to indicate the wide field of research which is open for the development of the quantitative relations of this interesting reaction in the light of recent discoveries, and particularly for the study of the functions of the peculiar form of "active chlorine" which characterizes the group, and which reacts with iodides in the proportional equivalent of $Cl = I_2$. What are the limits of its oxidizing activity? For example, it readily oxidizes iodides, arsenites and sulphites, but apparently will not bleach coloring matters. If it is conceded that the antiseptic value of hypochlorites is due to the formation of protein chloramines, what is the chemical explanation of the antiseptic action of the chloramines themselves either as formed in the tissues or as applied in the form of pharmaceutical preparations? The essential characteristic of the group is instability, and its relationship to the highly explosive nitrogen chloride would account for this. C. F. Cross patented the preparation of methylene chloramine from formaldehyde-ammonia,[6] which is also somewhat explosive, but it is recognized that certain classes of chloramines, including those of the nitrogenous colloids, are, comparatively speaking, stable compounds.

NOTE ON TRYPSIN, AND A NEW METHOD OF PURIFYING ENZYMES.[1]

By Joseph T. Wood, F.I.C.

In a paper entitled "A new method of isolating trypsin," L. Holzberg[2] refers to some work carried out by Robertson,[3] who found that when one drop of a saturated solution of safranine is added to 5 or 10 Cc. of neutral, or very faintly alkaline, 0.5 per cent. solution of Grübler's trypsin, a light, flocculent, colored precipitate slowly appears and gradually settles. It was assumed that the substance pre-

[6] Eng. Pat. 15,303 of 1909; *ibid.*, 1910, 976.

[1] Reprinted from *Journal of Society of Chemical Industry*, December, 1918.

[2] *J. Biol. Chem.*, 1913, 14, 335.

[3] *J. Biol. Chem.*, 1907, 2, 317.

cipitated by safranine is actually trypsin, since the supernatant liquid, although containing substances precipitated by alcohol, is practically free from enzymes. Holzberg has repeated Robertson's experiment. To solutions of Grübler's trypsin, Fairchild's trypsin, and aqueous extracts of sheep's pancreas, he added three eighths of the volume of a 0.8 per cent. solution of safranine. The precipitates were collected and washed, and their proteolytic action tested by digesting with a solution containing 2 Gms. of casein (Gross test). The results are given in the following summary: The substance which is precipitated by the addition of safranine to aqueous solutions of Grübler's or Fairchild's trypsin, or to aqueous extracts of pancreas, has a strong proteolytic action, contains safranine, is very sparingly soluble in water, and insoluble in organic solvents. After the substance has been removed from aqueous solutions of commercial trypsin or pancreas extract, a considerable quantity of a substance remains in solution, which is precipitable by alcohol, and in the case of pancreas extract, a further precipitate is obtained by means of an alcohol-ether mixture (three to one). These substances are practically devoid of preteolytic activity.

I repeated this experiment by adding a 0.1 per cent. and also a saturated solution of safranine to various infusions containing trypsin. An aqueous extract of the pancreas gave a considerable precipitate, which behaved in exactly the same way as the precipitate obtained by Holzberg. Instead of using the Gross test, I used the gelatin test.[4] I found it impossible to separate the precipitate from the filter, as it dried into a horny film. The paper was therefore cut up into small pieces, and in order to obtain some quantitative data it was cut into one-inch squares, which were weighed, and these were then ruled into 100 divisions and the small squares placed in the gelatin tubes. It was found that six squares liquefied, but five did not. The approximate weight of precipitate on one square inch, assuming it to be uniform, was 5.5 mgrms. The precipitate on 0.01 sq. in. would therefore be 0.055 mgrms., so that the quantity of dry precipitate which is active lies between 0.33 and 0.27 mgrm.

Since the whole of the gelatin was liquefied, it was evident that the substance causing the liquefaction was soluble, and it therefore seems that Holzberg, by washing his precipitate, has removed considerable quantities of enzyme. On repeating the experiments with one of my own trypsin preparations, which was comparatively free

[4] *Journal of Society of Chemical Industry*, 1912, 1105.

from albuminous matter, I was surprised to find that no precipitate was formed, *i. e.*, the ordinary preparations of trypsin, and aqueous extracts of pancreas, gave precipitates, but the purified preparation (the strength of which was equal to that of the crude preparation) gave no precipitate. It appears, therefore, that the matter precipitated by safranine is an albuminous compound, which carries the enzyme down with it, and that the precipitation by this method does not produce an enzyme-safranine compound. The method appears to be analogous to that used by Cohnhein[5] for the precipitation of diastase from saliva by means of calcium phosphate, in which a certain quantity of phosphoric acid was added to saliva and the liquid neutralized with lime water, which caused a copious precipitate of calcium phosphate. This precipitate carried down with it a large proportion of the proteins of the saliva, together with the diastase or ptyalin. The precipitate was then collected by filtration, and extracted with a volume of water equal to that of the saliva originally used. The diastase is slightly more soluble than the proteins, and accordingly passes into solution first. Conheim repeated this process several times, and finally precipitated the last extract by the addition of alcohol. This precipitate was collected, washed with alcohol, and dried over sulphuric acid, appearing then as an amorphous white powder, freely soluble in water. The author considered it to be free from proteins as its solution did not yield the usual reactions characteristic of these bodies.[6]

I have not yet had the opportunity to compare the nitrogen content of the purified trypsin with that of the trypsin before purification by the method I am about to describe. This would have an important bearing on the constitution of the enzyme.

On referring to Robertson's book on the proteins,[7] I find that, speaking of his own work two years earlier, he says, in the course of a discussion on the compounds of proteins with dyes, "I have found that in faintly alkaline solution trypsin or some constituent of Grübler's trypsin (nach Spalteholz) forms an insoluble compound with safranine"; from this it appears that Robertson himself was

[5] *Virchow's Archiv*, 1863, 28, 241. J. Reynolds Green, The Soluble Ferments (Camb. Univ. Press, 1899), p. 45.

[6] Since writing this paper the author has attempted to apply Cohnheim's method to trypsin, but has been unsuccessful.

[7] The Proteins (Univ. of California Publications in Physiology), October, 1909.

doubtful whether the precipitate was a compound of trypsin and safranine.

The method of purification of the enzyme which I adopted is a very simple one, and so far as I know has not been previously described; it depends on the fact that cellulose absorbs the impure compound of proteins and enzymes, and that after drying, the colloidal protein portion adheres firmly to the paper, whereas the enzyme is very easily soluble. The method is as follows:

Ordinary circles of Swedish filter paper (J. H. Munktell) 12½ cm. diam., area 122 sq. cm., ash 0.00095 Gm., averaging in weight 0.87 Gm. air-dry, were soaked in the impure enzyme solution, and dried quickly in a current of hot air. The average increase in weight was 0.054 Gm., *i. e.*, they contain about 6.0 per cent. of added matter, or 0.41 mgrm. per sq. cm. When such paper is placed in water, the enzyme dissolves quickly to a perfectly clear solution in a few minutes, but the colloidal matter with which it is associated adheres firmly to the paper; the solution is filtered after 15–20 minutes, by which time the whole of the enzyme matter is dissolved. If left for a longer time, proteins begin to dissolve, and the enzyme strength decreases.

When a solution of safranine is added to the enzyme solution prepared in this way, no precipitate is produced, and the solution passing through the filter is as active as the original solution, due account being taken of the dilution. The following experimental results were obtained: 1.8366 Gm. of the paper impregnated with enzymes was stirred in 183 Cc. of distilled water for 15 minutes, and then filtered; 0.6 Cc. of the filtrate was found to liquefy the standard gelatin tube under the same conditions as in the test previously described[8] corresponding to 6 mgrms. of the paper. The 6 mgrms. of paper contained 0.34 mgrm. of original extract.

A test of the original extract showed 0.35 mgrm. of matter capable of liquefying the gelatin, but the soluble matter is the 6 mgrms. of paper was found by evaporation of the filtrates to be 0.23 mgrm., so that the enzyme has been purified to this extent; *i. e.*, 35 per cent. of non-enzyme matter has been removed. For comparison it may be useful to give results for Grübler's pancreatin, which I have always used as a standard of comparison: it is labelled "Pankreatin Dr. G. Grübler & Co., Leipzig"; 0.1 Gm. dissolved in about 30 Cc. of alkaline water digests 8–10 Gms. of moist blood

[8] *Journal of Society of Chemical Industry*, 912, 1105.

fibrin; 0.52 mgrm. of the original solution liquefied, and 0.56 mgrm. filtered through paper liquefied, *i. e.*, my purified preparation is 2¼ times as strong as Grübler's trypsin. It may be noted that about 20 per cent. of the Grübler trypsin was insoluble in water.

I do not suppose for a moment that the preparation I have made is a pure enzyme, and I have not been able to ascertain how far the purification can be carried by the above method, but I have reason to believe that the purer the enzyme the less colloidal is its character, and that it will pass through a membrane. Professor Kipping has kindly examined a solution of the purified enzymes with the polariscope in order to ascertain if it is optically active. The solution contained 0.1184 Gm. of solids per 100 Cc., which was a strong solution from the point of view of enzyme activity, being about three times as strong as those I have usually employed. No rotation of the plane of polarization could be detected in a 200 Mm. tube. The following are the minimum quantities of material required to liquefy the gelatin in the test described:—Grübler's pancreatin (unfiltered), 0.56 mgrm.; do. (filtered), 0.52; safranine precipitate from pancreas extract, 0.30; pancreas extract on paper, 0.34; purified enzyme, 0.23 mgrm.

From the above facts I draw the conclusion that the enzyme itself is extremely soluble, whereas the protein matter with which it is associated is difficultly soluble, and this difference in solubility may be used to purify the enzyme.

DIGITALIS LEAVES: EFFECT ON ACTIVITY OF TEMPERATURE IN DRYING.[1]

By Herbert C. Hamilton.

Since the first attempt[2] to standardize digitalis leaves and the extracts, it has been observed that they vary greatly in activity.

Bennefield,[3] in 1881, using a method almost identical with that suggested in the 9th Rev. U. S. P. for standardizing the digitalis series of heart tonics found a variation of about 500 per cent. in the

[1] Reprinted from *The Journal of the American Chemical Society*, January, 1919. Contribution from the Research Laboratory of Parke, Davis & Co.

[2] *Ber.*, 40, 4586, 1907.

[3] Bennefield, "Ueber Digitalis Tincturen," Inaug. Diss., Göttingen, 1881.

activity of tinctures from digitalis leaves from various parts of Germany.

Bührer,[4] in 1900, found a difference of 400 per cent. in the activity of some fluidextracts. Fränkel[5] found variations of 300 to 400 per cent. in tincture and infusions. Edmunds,[6] in 1907, tested 17 commercial tinctures and found a variation of 400 per cent.

Many other similar results have been recorded, in some cases the reason being assigned to climate, soil, variety, or the locality from which the leaves were obtained.

Focke[7] observed that wild digitalis is more toxic than the cultivated and the second year's growth than the first. He also observed that the leaves gathered at seeding time are less active than when collected earlier. He was the first to record his observations as to the causes of deterioration and the effect of light and heat in drying the leaves. The former is negligible, but he considered that when dried in the air in the ordinary way without special care in preserving the activity is soon largely lost. This is considered to be due to the moisture content, which permitted the enzymes and ferments of the leaves to remain in an active state, and to their action in breaking down the sensitive glucosides to less active substances. His remedy is to heat the leaves rapidly to a temperature not to exceed 100°, drying to a moisture content of about ½ per cent. and preserving in dark air-tight jars.

Tordes,[8] in 1867, claimed that digitalis from the vicinity of Strassburg was better than that from other localities because of the careful selection, drying and preserving of the leaves. They used leaves of the second year's growth only, first dried in the shade, then in an oven at a temperature not over 40°. They were then kept in tin or glass containers away from light or moisture.

Sharp and Lancaster,[9] in a series of careful experiments, showed that digitalis leaves, not specially dried but kept dry, retained their activity for 11 years, while the fluid preparations began to deteriorate between the thirteenth and fifteenth months. They also observed that leaves of first-year plants were intensely bitter and probably very active.

[4] Bührer, Inaug. Diss., Basel, 1900.
[5] Fränkel, *Therap. Gegenw.*, 43, 106, 1902.
[6] Edmunds, *J. Am. Med. Assoc.*, 48, 1744, 1907.
[7] Focke, *Arch. Pharm.*, 245, 646, 1907.
[8] Tordes, *Gaz. Med. Strassburg*, 27, 191, 1867.
[9] Sharp and Lancaster, *Pharm. J.*, 32, 102, 1911.

Hatcher and Eggleston[10] found that old samples of digitalis leaves and tinctures, neither of them specially preserved, were not much below their original activity. They concluded that fluid preparations containing not less than 50 per cent. alcohol do not deteriorate to any considerable degree. This, however, is not in accord with most investigators, although the higher strengths of alcohol are in general much better for preserving the activity.

Houghton and Hamilton,[11] in a series of tests and retests of digitalis extracts, showed that none of them is free from the fault of deterioration, their results pointing to the apparent fact that the higher percentages of alcohol not only more completely extract but also more thoroughly preserve the active principles.

On the supposition that the strong alcohol destroys the active ferments these results are in accord with the results of Perrot and Goris,[12] who published a method by which the enzymes could be destroyed with the subsequent complete preservative of the drug in its original activity. This was accomplished by subjecting the drug to the vapors of boiling alcohol after which it was dried in the air. Such precautions, however, seem unnecessary in view of the results with old samples of digitalis obtained by the different investigators quoted, especially Hatcher, who found high values in 25-year-old leaves, and Sharp and Lancaster, who found 11-year-old drug to have lost little of its activity.

The writer recently had occasion to extract and test a sample which had been in the possession of Northwestern University for twenty-five years. Its activity was fully 150 per cent. of that of the average drug at present obtainable.

Recently the subject of drying digitalis leaves has come up in connection with the samples of this drug grown wild in Oregon and submitted to the government for the Medical Department of the Army. It was stated that unless the drug was dried in an oven, at 75 to 90°, it was practically worthless.

This statement being so entirely at variance with the opinions commonly held, some experiments were inaugurated to demonstrate its correctness. Unfortunately, there was not available a sufficient amount of the growing digitalis leaves to make the experiments con-

[10] Hatcher and Eggleston, *Am. J. Pharm.*, 85, 203, 1913.
[11] Houghton and Hamilton, *ibid.*, 81, 461, 1909.
[12] Perrot and Goris, Abs. in *La Presse Medicale*, 17, 776, 1909.

clusive but the results are apparently of sufficient importance to be published.

From some previous experiments, unpublished, it has been observed that the fresh leaves extracted with 95 per cent. alcohol had a higher degree of activity than the average digitalis on the market and apparently the tincture, so prepared, was more active than that prepared from a part of the same lot of leaves dried before extraction.

The following experiments were, therefore, planned and carried out. Fresh leaves were gathered from the flowering and fruiting plants in July, divided into three equal amounts and extracted as follows:

First: Extracted immediately with 95 per cent. alcohol for the moistening and then with 70 per cent. alcohol to complete exhaustion.

Second: Dried in an oven at temperatures ranging between 75° and 90°, then extracted with 70 per cent. alcohol. The drying covered a period of about 5 hours.

Third: Dried in the air and partly in the sun over a period of 4 days, then extracted with 70 per cent. alcohol.

The tinctures were made to the same amount on the basis of the weight of the oven-dried lot, which was considerably less than that of the air-dried sample.

Only two lots of drug were available, one being the official variety *digitalis purpurea,* and the other a non-official variety.

The results of essays are as follows, the method of testing being the M. L. D. method originally applied by Houghton.[18] The correctness of the end result was in every case checked by examining the heart of the dead frog to determine whether death occurred with heart in systole—the characteristic position from digitalis poisoning.

These results coincide with those previously obtained in that the fresh drug has greater toxicity than the dried. The experiments also show that the high temperature employed in the oven caused a greater immediate deterioration than the slower drying at the season temperatures.

Further experiments are planned to demonstrate whether the oven-dried drug is more stable than the air-dried sample but this point could not be considered, as not sufficient leaves were available

[18] Houghton, *J. Am. Med. Assoc.,* 31, 959, 1898.

TABLE I.

DIGITALIS PURPUREA FROM A FLOWER GARDEN IN DETROIT.

Not Dried.			Oven Dried.			Sun / Air } Dried.		
Weight.	Dose.	Result.	Weight.	Dose.	Result.	Weight.	Dose.	Result.
22	0.004	Alive	16.5	0.010	Alive	19	0.010	Dead
22	5	"	10.5	0.012	Dead	19	0.012	"
22.5	6	"	16.5	0.015	"	19.5	0.015	"
22.5	7	"	14	0.020	"	20.5	0.018	"
23	8	Dead	13.5	0.025	"	20.5	0.022	"
23.5	0.0045	Alive	23	0.008	Dead	24	0.007	Alive
25	55	"	24	0.010	"	24.5	0.008	"
25	65	"	24	0.012	"	24.5	0.009	Dead
25	75	Dead	24	0.014	"	25	0.010	"
26	0.0090	"	24	0.016	"	26	0.011	"
27	0.0055	Alive	20	0.006	Alive	22	0.007	Alive
27	65	"	20	0.007	"	22.5	0.008	"
27.5	75	"	21	0.008	"	23	0.009	Dead
29.5	85	Dead	21	0.009	"	24	0.010	"
30	0.01	"	21	0.010	Dead	26	0.011	Alive
27	0.0070	Alive	24.5	0.008	Alive	25.5	0.008	Dead
29.5	75	"	25	0.009	Dead	25.5	0.009	"
29.5	75	"	25.5	0.010	Alive	26	0.010	"
30.5	80	Dead	25.5	0.011	Dead	26	0.011	"
33	80	"	25.5	0.012	"	26	0.012	"

Summarizing the above.

0.007 killed none of 3	0.008 killed 1 of 3	0.008 killed 1 of 3
0.0075 killed 1 of 4	0.009 killed 1 of 2	0.009 killed 3 of 3
0.008 killed 3 of 3	0.010 killed 2 of 4	0.010 killed 4 of 4
	0.011 killed 1 of 1	0.011 killed 2 of 3
	0.012 killed 3 of 3	0.012 killed 2 of 2
Activity 153	100	133
H. T. U. ..... 9+	6	8
M. L. D. 0.008	0.011	0.009
Activity in terms of undried drug 100%	72	81

to make the experiment conclusive. Such experiments should be continued over a period not less than three years.

In further consideration of the previously mentioned criticism against the Oregon air-dried leaves it should be noted that the method of testing was also called in question. On this point, while there is wide divergence of opinion as to which of several methods shows the real value of the drug, there is quite general agreement on the frog as the test animal, and until clinical evidence is brought

forward to negative the results it is logical to assume that the death of the frog with heart in systole, or the stoppage of the heart in systole in one hour is a satisfactory measure of the activity of a digitalis preparation. Compared with the guinea-pig method of Reed and Vanderkleed[14] and the Hatcher cat method,[15] both of which are purely toxicity methods, the frog methods have the advantage that deaths from other than digitalis poisoning are eliminated and form no part of the record.

TABLE II.

DIGITALIS LEAVES NON-OFFICIAL FROM A GARDEN ON GROSSE ILE, MICH.

Not Dried.			Oven Dried.			Sun / Air Dried.		
Weight.	Dose.	Result.	Weight.	Dose.	Result.	Weight.	Dose.	Result.
17	0.004	Dead	20	0.004	Dead	23.5	0.002	Alive
18.5	0.005	"	27	0.005	"	25	0.003	Dead
19.5	0.006	"	23.5	0.006	"	25	0.004	"
27.5	0.007	"	23.5	0.007	"	25.5	0.005	"
18	0.0010	Alive	21	0.0010	Alive	19.5	0.0010	Alive
19	0.0020	Dead	22	0.0020	"	20	0.0015	"
19	0.0030	"	22.5	0.0030	"	20.5	0.0020	"
19	0.0040	"	25	0.0040	"	21.5	0.0025	"
20	0.0050	"	27.5	0.0050	Dead	22.5	0.0030	"
18	0.0010	Alive	23	0.0035	Dead	30	0.0025	Alive
19.5	0.0015	Dead	23	0.0040	"	28	0.0030	Dead
20.5	0.0020	"	23	0.0045	"	28	0.0035	"
21	0.0025	"	23.5	0.0050	"	29	0.0040	"
21	0.0030	"	23.5	0.0060	"	30	0.0045	"
			22.5	0.0020	Alive			
			23	0.0025	"			
			25	0.0030	"			
			27	0.0033	Dead			
			27.5	0.0040	"			

M. L. D.	0.0015	0.0035	0.0030
H. T. U.	44	19	22
Per cent. activity ..	730	310	370
Activity compared to undried	100%	42	50

One may conclude, therefore, that oven drying has no advantage over a reasonably rapid air drying of digitalis leaves, and that the drying causes a marked deterioration, no products more highly toxic

[14] Reed and Vanderkleed, *Am. J. Pharm.*, 80, 110, 1908.

[15] Hatcher and Brody, *ibid.*, 82, 369, 1910.

than those present in the crude drug having been developed during the process of drying.

RESEARCH LABORATORY, PARKE, DAVIS & CO.,
DETROIT, MICH.

MELTING POINT OF ROSIN.[1]

BY T. LINSEY CROSSLEY.

Centain large buyers of rosin have recently specified a melting point limit for this material. Samples have been submitted for this test, but without specifying how the test was to be carried out.

Properly speaking, rosin, like asphalt, has no definite melting point, therefore, any specification aiming to grade it by reference to its behavior on heating should state the method for obtaining results.

Schwalbe and Kuderlinn[2] not only state melting points, but record results to fractions of one degree and claim to differentiate between certain rosins by their melting points.

Several methods have been used to determine the quality of rosin as indicated by its action on heating. The closed capillary tube, of such general application, is used largely but, unless conditions of heating and observation are closely controlled, results are not uniform with different operators.

The following results were obtained on the same four samples by methods indicated:

Rosin.	¼" Column. ° F.	⅛" Column, ° F.	Film, ° F.	Capillary, ° F.
1.....	174–184	169–172	150	146
	172–183	169–172	146	145
	.....	165–173	...	154[3]
2.....	176–187	174–182	147	154
	174–185	167–176	155	147
	.....	.....	156	153
3.....	161–167	149–151	120[4]	128
	161–157	145–146	134	130
	.....	.....	126	...
4.....	153–155	145–147	135	138
	147–155	144–145	133	136
	149–153	.....	...	...

[1] Reprinted from the *Jour. of Indust. and Engr. Chem.*, January, 1919.

[2] "Rosin Studies," *J. Soc. Chem. Ind.*, 30, 1397.

[3] Heated until clear.

[4] Probably mechanical weakness of film.

The first three methods were carried out as follows: Glass tubes of about $\frac{3}{16}$ in. inside diameter and 2 in. long were prepared. These were dipped in melted rosin so that on cooling there was left inside the tube a column of rosin of the required depth. In the case of the method marked "film" the foot of the glass tube was heated slightly and applied carefully to the surface of the molten rosin so that upon cooling a thin film only of the rosin was formed. The tubes were attached to the thermometer in such a way that the bottom of the tube with the rosin was located about the center of the mercury bulb. The thermometer with tube attached was immersed in cold water in a 400 Cc. beaker with the bottom of the rosin column 1 in. below the surface. The temperature was raised about 3° per minute.

In the cases of ¼ in. and ⅛ in. columns, it will be noted that two temperatures are given. The lower temperature indicates the point at which the rosin is soft enough for the water to enter the tube, the other being the point at which the water breaks through. The result is of course merely the point at which the viscosity is so reduced that it is overcome by the pressure of 1 in. of water. It is necessary that the heating should be well regulated. If heat is applied too rapidly it will naturally result in a higher final temperature and a wider spread between the two points.

The capillary tube method was carried out as follows: Tubes about 1 Mm. in diameter were prepared and sealed at one end. The rosin was pulverized between two pieces of paper. About 2 Cm. of the tube were filled with the powder, and it was attached to the thermometer as in the other cases, being also immersed in cold water and heated as before.

A reading glass was used to observe the result and the point at which the particles coalesced was noted as the melting point. It was not found advisable to carry the heating until the whole of the rosin in the tube became clear as this increased the range of personal error. There was found to be a more definite indication and closer agreement when the point of coalescence was noted.

The results obtained by the "film" method are for practical purposes the same as those obtained by the "capillary" method, but the tests are prepared more rapidly and with much less trouble, especially in the hands of unskilled assistants. The end-point is definitely established by the penetration of the water.

In all of these tests recently boiled water should be used, otherwise the rising bubbles of dissolved gases interfere in several days.

43 Scott Street,
Toronto, Canada.

CORRESPONDENCE.

THE COMMITTEE OF REVISION OF THE UNITED STATES PHARMACOPŒIA 1910–1920.

The Next Pharmacopœia.

May, 1920, only a little more than a year hence, will again witness the assembling in Washington of the delegates to the United States Pharmacopœial Convention. This fact should stimulate preconvention activity on the part of those who have had experience with the present revision and are prepared to suggest improvements for a new edition.

It is desirable at this time that pharmacists, physicians, chemists, botanists, biological experts, or any others who use the U. S. P. IX. should submit to the chairman of the Revision Committee either personally or through associations, such helpful information as their experience may have suggested, or which may have come to their attention.

These suggestions will be compiled systematically and circularized to the present Revision Committee, the authors being credited in each instance with the recommendations, and the compilation will be submitted to the 1920 convention for the benefit of the new Committee of Revision.

You are earnestly urged to coöperate with the Committee of Revision in the preparation of this report and it is requested that in sending in your suggestions, the special form enclosed be employed. Please use a *separate sheet* for *each subject.* As many forms as are desired will be mailed on request.

Respectfully submitted,

Charles H. LaWall,

Chairman of the Committee of Revision of the United States Pharmacopœia.

UNITED STATES PHARMACOPŒIA.

Suggestions for the U. S. P. X.

(Use a separate sheet for each subject: additional sheets may be obtained from the chairman, Charles H. LaWall, 39 S. Tenth Street, Philadelphia, Pa.)

Subject Discussed .....

Brief Abstract of Recommendation .....

Details .....

Reasons for Proposal .....

Date .....

Signature .....

Address .....

CONCERNING THE INFLUENCE OF STEMS AND ROOTS UPON THE ALKALOIDAL CONTENT OF STRAMONIUM.

New York, N. Y., Feb. 18, 1919.

DR. GEO. P. KOCH,
Care of H. K. Mulford Co.,
Glenolden, Pa.

Dear Sir: I found your article in the AMERICAN JOURNAL OF PHARMACY, January, 1919, on the alkaloidal content of stems, roots and leaves of stramonium quite interesting and instructive.

I would be glad to have a little further information regarding the samples identified as 223–4 and 5. I would assume from the statements on page 13 that these represent composites of samples nos. 211–12 and 13 with 10 per cent. of samples nos. 214–15 and 16. It is at once evident, however, that my understanding is not correct or that there has been a misprint.

If 10 per cent. of samples nos. 214–15 and 16 were added to samples nos. 211–12 and 13 in the order indicated, the resulting mixtures would assay approximately 0.55, 0.56 and 0.40.

I note that you refer to the 10 per cent. foreign material as "inert." It occurs to me, therefore, that possibly primary stems instead of secondary stems as stated was the material used, as this is relatively inert, while the secondary stems, as you have shown, could not be considered "inert" in comparison with the leaves.

It is possible that other readers may have found the same difficulty that I have found and possibly publication of the explanation would be found useful by others as well as myself.

Respectfully,

A. G. MURRAY,
Assistant Chemist.

February 24, 1919.

DR. A. G. MURRAY,
Room 1034, U. S. Appraiser's Stores,
Christopher and Washington Sts.,
New York City, N. Y.

Dear Sir: I have your letter of the 18th instant, relative to my paper on stramonium, which appeared in the January issue of the AMERICAN JOURNAL OF PHARMACY.

Samples were made by adding to the dry unground secondary stems, nos. 214, 215 and 216 to samples of dry leaves, nos. 211, 212 and 213, respectively, so that the former furnished 10 per cent. and the latter, 90 per cent. of the whole. These samples were made when the materials were in the *whole* condition, that is, before being ground for analysis. It is true, if 10 per cent. of the ground samples of nos. 214, 215 and 216 was added to nos. 211, 212 and 213, respectively, the resulting mixtures should certainly have assayed approximately, 0.55, 0.56 and 0.40 per cent., respectively, as you suggest. However, in making samples using the pieces of stems in the unground condition as before mentioned, due to the natural variation of the individual parts of the plants, it would be quite impossible to expect the analytical results to be as mathematically calculated. I must attribute the variation of these results to this fact of the variation of the individual parts of the plants, since the whole (unground parts) of these samples were mixed, then ground and mixed well for analysis.

In carrying out this experiment, it was not my intention to test the analytical method, but make mixtures of unground parts of the plants as nearly as possible as they would occur under practical

conditions, and find out if the mixtures were still fulfilling the United States Pharmacopœia requirement with regard to strength.

With reference to the 10 per cent. foreign material which was employed—10 per cent. of secondary stems were used as shown in the text of the article on page 13, line 16. My purpose in taking 10 per cent. of secondary stems was again for a practical consideration. If stems are considered foreign material by the United States Pharmacopœia in harvesting by picking the leaves or cutting the upper parts of the plant with a knife, we would be more apt to gather the secondary stems in conjunction with the leaf, than the primary stems.

It is true, from the results of the determinations as presented in table IV., page 14 of the article, secondary stems could hardly be considered "inert," or foreign material either, for that matter.

Regarding the accuracy of preparing the samples and the work in grinding the samples for analysis, and making the analytical determinations, very great care was manifested in every phase of the work. The analytical work was checked gravimetrically and volumetrically.

I am very glad that this matter has been called to my attention and your letter and a copy of my reply will be placed in the hands of the publishers as you suggested.

Very truly yours,

GEORGE P. KOCH,
Agricultural Chemist.

COLLEGE NOTES.

FIRST NAVAL HOSPITAL UNIT AT P. C. P. CLOSES ITS WORK.—On Thursday evening, February 13, there was held in the Auditorium and Museum of the college the closing exercises of the U. S. Naval Hospital Corpsmen who had completed a three months' course of intensive training in the U. S. Naval Hospital Corps Training School of the Philadelphia College of Pharmacy.

Addresses were made by Admiral Hughes, Commandant of the Philadelphia Navy Yard and Ex-Governor Edwin S. Stuart.

One hundred and sixty-two men were in the unit at its beginning, but a number had been transferred or discharged during the three months. Certificates were awarded to the men who had satis-

factorily completed the course which comprised the fundamentals of pharmacy, chemistry, microscopy, first aid and instruction in typewriting given on two evenings of each week at the Peirce School.

It has been planned by the Navy Department to follow the first unit immediately by a second group of one hundred and fifteen men who will take a three or four months' special course.

THE P. C. P. IN THE MILITARY SERVICE.—The termination of the war found more than 500 students and alumni of the college wearing khaki uniforms. Eighteen are known to have laid down their lives on the altar of liberty and the first American enlisted man to die on "Flanders Fields" was Kenneth B. Hay, who at the time of his enlistment was a junior student at the college.

Dr. John A. Roddy, professor of bacteriology, is now a major in the medical service of the army, and is stationed in Oklahoma.

Mr. Ralp Foran has received his honorable discharge from the Chemical Warfare Service of the army and has returned to the college and resumed the position of assistant in the Analytical Chemical Laboratory.

Prof. Robert P. Fischelis, having been released from the Gas Warfare Service, has taken up his duties with Messrs. H. K. Mulford Company and resumed his lectures at the college.

Mr. Donald Margerum, a graduate of the Course in Food and Drug Chemistry at the college, and formerly an assistant to Prof. Charles H. LaWall in his private chemical laboratory, is now bacteriologist in a debarkation camp in Virginia.

Mr. Leon Claire, a member of the class of 1917, was officially cited for "conspicuous bravery" while serving as an ambulance driver in the Italian-Alpine section. He was trained at the famous Allentown, Pa., ambulance encampment. His brother, Captain Fred Claire, who had also attended the college for a short time, was one of the first American medical officers to lose his life at the front.

When the "Haverford" docked at the Port of Philadelphia, the

only returning Philadelphia soldier was W. Seimon, a graduate of the class of 1911, who volunteered early in the war and had seen active service abroad for over a year.

The college is preparing to do its share in helping discharged soldiers and sailors to locate themselves in the drug business or in some other civilian line of activity. A committee of the college under the chairmanship of Prof. Freeman P. Stroup is actively engaged in this service.

It has been proposed that the Philadelphia College of Pharmacy shall present to each student and alumnus who has served in the army or navy in the World War a suitably designed bronze medal as an evidence of appreciation for his services in behalf of the nation and as a token of honor and distinction.

"The Corn Exchange" Commends the College.—*The Corn Exchange,* a magazine published by the Corn Exchange National Bank of Philadelphia, which has more than a local circulation, recently published a well-written article on the history of the Philadelphia College of Pharmacy and its record of achievements.

Prof. Robert P. Fischelis Lectures on Gas Warfare.—Prof. Robert P. Fischelis has recently lectured before meetings of the New York Branch and the Philadelphia Branch of the American Pharmaceutical Association describing the methods of gas warfare and the problems, both offensive and defensive, which this had created. He also delivered a similar address before the Philadelphia Association of Credit Men at their recent meeting at the Ritz-Carlton Hotel.